



A 28-year-old woman is brought to the emergency department by her family due to acute left flank pain. The pain radiates to her groin and is associated with pink hematuria and urinary urgency. Past medical history is unremarkable, and the patient has never experienced similar symptoms. CT scan of the urinary system confirms the presence of a stone at the ureterovesical junction. The patient is given intravenous morphine sulfate for pain relief. Fifteen minutes later, she develops diffuse itching involving the arms, legs, and back. Which of the following is the most likely mechanism causing this patient's adverse reaction?

- ☐ A. IgE-dependent mast cell degranulation
- ☐ B. IgE-independent mast cell degranulation
- ☐ C. Inhibition of prostaglandin synthesis
- ☐ D. Precipitation of immune complexes
- ☐ E. T cell release of inflammatory cytokines

**Submit**





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- ☐ A. IgE-dependent mast cell degranulation (57%)
- ☒ B. IgE-independent mast cell degranulation (36%)
- ☐ C. Inhibition of prostaglandin synthesis (1%)
- ☐ D. Precipitation of immune complexes (2%)
- ☐ E. T cell release of inflammatory cytokines (2%)

Correct



36%

Answered correctly



39 secs

Time Spent



01/16/2021

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This patient with acute pruritus following administration of morphine most likely has medication-induced **IgE-independent** mast cell activation. A number of medications, including **opioids**, **radiocontrast agents**, and some antibiotics (eg, **vancomycin**), can induce mast cell degranulation by activation of protein kinase A and PI3 kinase. This results in release of several mediators, including histamine, bradykinin, heparin, and a number of enzymes and chemotactic factors. Common symptoms include diffuse itching and pain, bronchospasm, and localized swelling (**urticaria**).

**(Choice A)** IgE-mediated degranulation is typically associated with environmental exposures such as foods or vespid stings or with medications such as beta-lactam and sulfonamide antibiotics. Opioids can cause IgE-dependent degranulation (very rare), but IgE-independent reactions are more common.

**(Choice C)** Inhibition of cyclooxygenase 1 by aspirin and nonsteroidal anti-inflammatory drugs can trigger urticaria in patients with chronic idiopathic urticaria. These medications shunt arachidonic acid metabolites toward formation of leukotrienes, which increase vascular permeability.


**(Choice D)** Serum sickness is a type III hypersensitivity reaction caused by precipitation of circulating immune complexes. Typical symptoms include fever, pruritic **rash**, and arthralgias starting 7-14 days after antigen exposure. Common triggers include beta-lactam and sulfonamide antibiotics.

**(Choice E)** Acute allergic contact dermatitis is caused by a T cell-mediated type IV (delayed)



This patient with acute pruritus following administration of morphine most likely has medication-induced

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This patient with acute pruritus following administration of morphine most likely has medication-induced

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**(Choice D)** Serum sickness is a type III hypersensitivity reaction caused by precipitation of circulating immune complexes. Typical symptoms include fever, pruritic [rash](#), and arthralgias starting 7-14 days after antigen exposure. Common triggers include beta-lactam and sulfonamide antibiotics.

**(Choice E)** Acute allergic contact dermatitis is caused by a T cell-mediated type IV (delayed) hypersensitivity reaction to an antigen on the skin surface. Gross findings include erythematous, papulovesicular, weeping [lesions](#).

### Educational objective:

A number of medications, including opioids, radiocontrast agents, and some antibiotics (eg, vancomycin), can trigger IgE-independent mast cell degranulation. Common symptoms include diffuse itching and pain, bronchospasm, and localized swelling (urticaria).

### References

- [Pharmacological stimuli in asthma/urticaria.](#)
- [Pathogenic intracellular and autoimmune mechanisms in urticaria and angioedema.](#)
- [Codeine induces human mast cell chemokine and cytokine production: involvement of G-protein activation.](#)

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A 31-year-old male farm worker comes to the physician complaining of an itchy rash on his chest. Physical examination reveals an annular and scaling plaque five centimeters in diameter with central clearing on the chest. KOH preparation of skin scrapings shows branching septate hyphae, and topical application of terbinafine was prescribed. Which of the following mechanisms of action explains the antifungal activity of this drug?

- ☐ A. Binding to ergosterol
- ☐ B. Inhibition of squalene epoxidase
- ☐ C. Blocking  $\beta$ -D-glucan synthesis
- ☐ D. Preventing mitosis by binding tubulin
- ☐ E. Inhibition of fungal protein synthesis

**Submit**



A 31-year-old male farm worker comes to the physician complaining of an itchy rash on his chest. Physical examination reveals an annular and scaling plaque five centimeters in diameter with central clearing on the chest. KOH preparation of skin scrapings shows branching septate hyphae, and topical application of terbinafine was prescribed. Which of the following mechanisms of action explains the antifungal activity of this drug?

- ☐ A. Binding to ergosterol (15%)
- ✓ ☒ B. Inhibition of squalene epoxidase (59%)
- ☐ C. Blocking  $\beta$ -D-glucan synthesis (7%)
- ☐ D. Preventing mitosis by binding tubulin (8%)
- ☐ E. Inhibition of fungal protein synthesis (9%)

Correct



59%

Answered correctly



01 min, 19 secs

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The patient described in this vignette is presenting with symptoms of tinea corporis. Clinically tinea corporis presents as an annular scaling plaque with well-demarcated, raised erythematous borders and central clearing.

Terbinafine is a commonly used drug for treatment of dermatophytosis. It belongs to the class of antifungals called allylamines and may be used topically or orally. Terbinafine inhibits synthesis of ergosterol of the fungal membrane by inhibiting the enzyme squalene epoxidase. Ergosterol is a cell membrane sterol that is unique to fungi and does not occur in human cell membranes. This drug tends to accumulate in skin and its appendages, and its side effects are mild by the topical route.

**(Choice A)** Binding to ergosterol is a mechanism of action of polyene antifungals (amphotericin B and nystatin).

**(Choice C)** Caspofungin belongs to the echinocandin class of antifungals. It blocks synthesis of  $\beta$  (1,3)-D-glucan, a main component of *Candida* and *Aspergillus* cell walls.

**(Choice D)** Griseofulvin binds to polymerized microtubules and disrupts the fungal mitotic spindle, thus preventing fungal cell mitosis. It accumulates in the skin and its appendages and is only effective in



membrane sterol that is unique to fungi and does not occur in human cell membranes. This drug tends to accumulate in skin and its appendages, and its side effects are mild by the topical route.

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**(Choice D)** Griseofulvin binds to polymerized microtubules and disrupts the fungal mitotic spindle, thus preventing fungal cell mitosis. It accumulates in the skin and its appendages and is only effective in dermatophytosis.

**(Choice E)** Flucytosine is an antimetabolite antifungal that is transformed into 5-fluorouracil in the fungal cell. It inhibits fungal protein synthesis by replacing uracil with 5-fluorouracil in fungal mRNA. It is used in systemic fungal infections.

**Educational Objective:**

Terbinafine is used for treatment of dermatophytosis. It inhibits synthesis of fungal membrane ergosterol by suppressing the enzyme squalene epoxidase.



A 17-year-old boy comes to the office due to a facial lesion. The patient noticed a small area of rough skin on his lower lip several weeks ago, which has progressively enlarged. He reports no pain or itching. The patient had eczema during early childhood but has had no other chronic medical conditions. Vital signs are within normal limits. Physical examination findings are shown in the [exhibit](#). There are no other skin rashes, oral lesions, or enlarged lymph nodes. Which of the following histopathological findings are most likely present in this patient's skin lesion?

- ☐ A. Acantholysis and multinucleated giant epithelial cells
- ☐ B. Epidermal hyperplasia and cytoplasmic vacuolization
- ☐ C. Subcorneal bacterial collection and neutrophilic infiltration
- ☐ D. Subepidermal linear complement deposits and separation

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A 17-year-old boy comes to the office due to a facial lesion. The patient noticed a small area of rough skin on his lower lip several weeks ago, which has progressively enlarged. He reports no pain or itching. The patient had eczema during early childhood but has had no other chronic medical conditions. Vital signs are within normal limits. Physical examination findings are shown in the [exhibit](#). There are no other skin rashes, oral lesions, or enlarged lymph nodes. Which of the following histopathological findings are most likely present in this patient's skin lesion?

- ☐ A. Acantholysis and multinucleated giant epithelial cells (27%)
- ☒ B. Epidermal hyperplasia and cytoplasmic vacuolization (65%)
- ☐ C. Subcorneal bacterial collection and neutrophilic infiltration (3%)
- ☐ D. Subepidermal linear complement deposits and separation (3%)

Correct



65%

Answered correctly



02 mins, 10 secs

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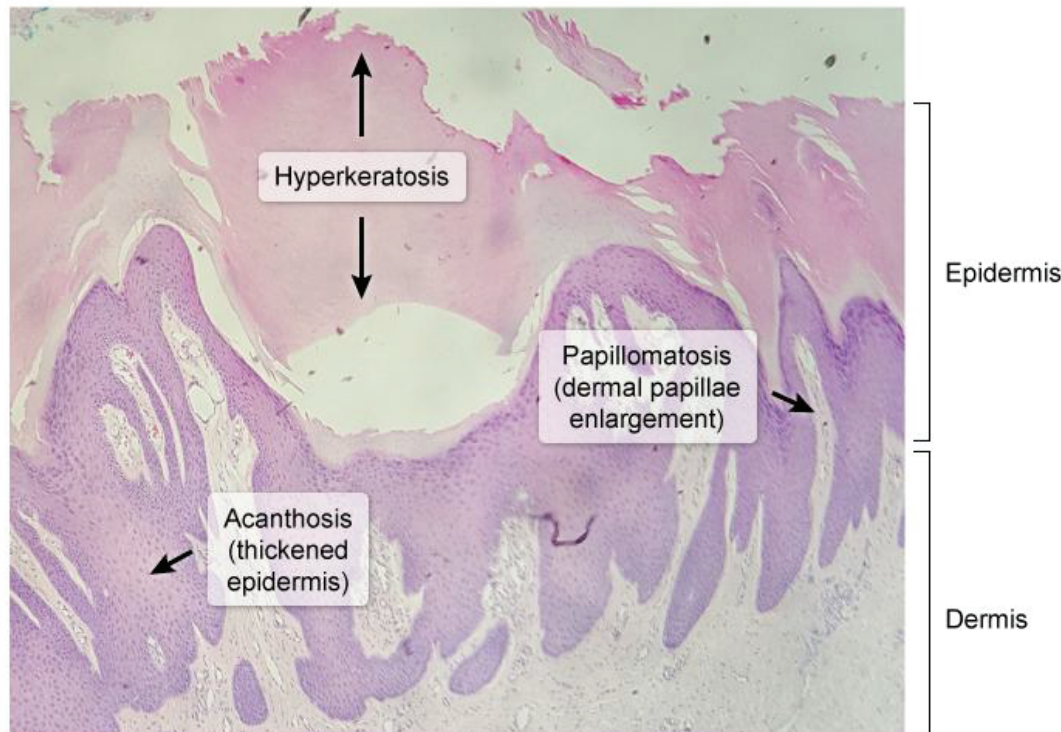


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### Verruca vulgaris





This patient has a common **cutaneous wart** (ie, verruca vulgaris). Cutaneous warts are caused by **human papillomavirus**, which also causes anogenital warts (ie, condyloma acuminata). The virus is usually transmitted by direct contact and is most common in children, adolescents, and young adults.

Cutaneous warts typically present as **skin-colored papules** or well-circumscribed plaques. They may also form complex **filiform lesions**. On the palms or soles (ie, palmar, plantar warts), they commonly present as tender plaques or **nodules** that disrupt the normal skin striae.

The diagnosis of cutaneous warts is often apparent based on gross findings. Key findings on magnified view (ie, dermoscopy) include a roughened surface and **small black dots** representing **thrombosed capillaries**. Biopsy is usually not needed but can confirm the diagnosis in atypical cases. Histopathologic findings include:

- **Epidermal hyperplasia** (acanthosis) with eosinophilic inclusions and keratohyaline granules
- Thickened stratum corneum (**hyperkeratosis**)
- **Papilloma** formation
- Perinuclear **cytoplasmic vacuolization** (**koilocytosis**)

**(Choice A)** Intraepidermal fracturing (acantholysis) and formation of multinucleated cells are seen in





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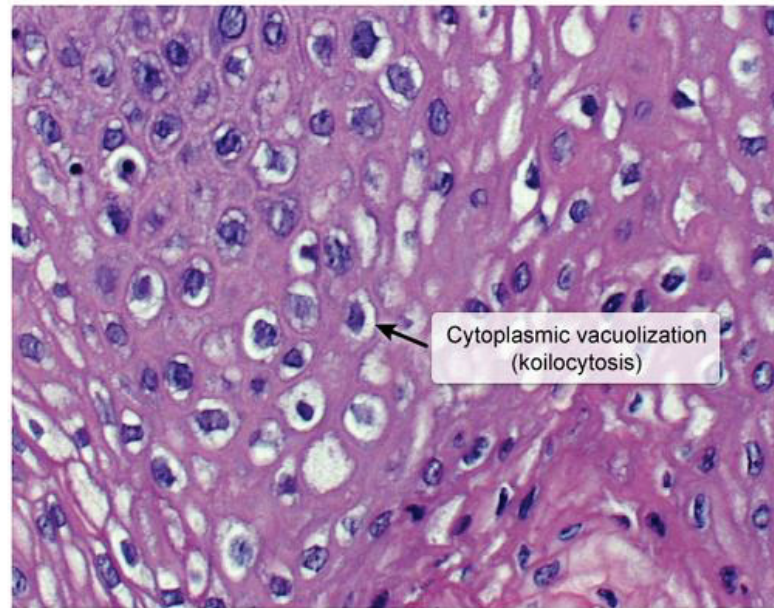
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## Verruca vulgaris



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- Perinuclear **cytoplasmic vacuolization** ([koilocytosis](#))

**(Choice A)** Intraepidermal fracturing (acantholysis) and formation of multinucleated cells are seen in herpes simplex labialis. Although this condition is often found on the lips and perioral skin, it presents with acute/recurrent [blisters and ulcers](#).

**(Choice C)** Impetigo is a gram-positive skin infection that generates a neutrophilic infiltrate. It presents with erythema, blistering, and shallow ulcers with [honey-colored crusts](#).

**(Choice D)** Bullous pemphigoid is an autoimmune disorder associated with antibodies against hemidesmosomes, leading to subepidermal complement activation and cleavage. It is most common at age >60 and typically presents with pruritic [plaques, erosions, and tense bullae](#).

### Educational objective:

Cutaneous warts (ie, verruca vulgaris) are caused by human papillomavirus and typically present as rough, skin-colored papules. If necessary, biopsy can confirm the diagnosis and shows epidermal hyperplasia, thickened stratum corneum, papilloma formation, and cytoplasmic vacuolization.

### References

- [Benign epithelial oral lesions - association with human papillomavirus](#).



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A 22-year-old man comes to the office due to skin lesions. The patient noticed a nonpainful, nonpruritic skin bump on his right knee 3 months ago, which progressively increased in size and number. He has no prior health issues and takes no medications. The patient is outdoors frequently for work and recreational activities. He is sexually active. Physical examination findings are shown in the [exhibit](#). Which of the following microbial organisms is most likely responsible for this patient's current condition?

- ☐ A. Coxsackievirus
- ☐ B. Herpes simplex virus
- ☐ C. Human papillomavirus
- ☐ D. *Neisseria gonorrhoeae*
- ☐ E. Pox virus
- ☐ F. *Treponema pallidum*

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- ☐ A. Coxsackievirus (1%)
- ☐ B. Herpes simplex virus (3%)
- ☒ C. Human papillomavirus (53%)
- ☐ D. ~~Neisseria gonorrhoeae~~ (2%)
- ☐ E. Pox virus (35%)
- ☐ F. ~~Treponema pallidum~~ (3%)

Correct



53%

Answered correctly



01 min, 33 secs

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11/04/2020

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**Cutaneous warts (verruca vulgaris)**

<b>Etiology</b>	<ul style="list-style-type: none"><li>• Human papillomavirus</li><li>• Acquired by direct contact</li></ul>
<b>Appearance</b>	<ul style="list-style-type: none"><li>• Plaques, papules, verrucous lesions</li><li>• Skin, nail folds, palms/soles</li><li>• Thrombosed capillaries on magnified view</li></ul>
<b>Histopathology</b>	<ul style="list-style-type: none"><li>• Thickening of stratum corneum</li><li>• Epidermal hyperplasia &amp; papilloma formation</li><li>• Cytoplasmic vacuolization (koilocytosis)</li></ul>
<b>Natural history</b>	<ul style="list-style-type: none"><li>• Gradual, chronic course</li><li>• Spontaneous resolution (usually &lt;2 years)</li><li>• Possible recurrence</li></ul>

This patient has **cutaneous warts** (verruca vulgaris), presenting as painless, **skin-colored papules** with a dry, whitish surface. Warts may be single or multiple and can also form **irregular plaques** or complex **filiform structures**. The diagnosis of cutaneous warts is usually made on inspection, although a magnified

This patient has **cutaneous warts** (verruca vulgaris), presenting as painless, **skin-colored papules** with a dry, whitish surface. Warts may be single or multiple and can also form **irregular plaques** or complex **filiform structures**. The diagnosis of cutaneous warts is usually made on inspection, although a magnified view (ie, dermatoscopy) can be helpful and typically reveals small black dots representing thrombosed capillaries.

Cutaneous warts are caused by **human papillomavirus** (HPV), which is also the cause of **plantar warts** and **anogenital warts** (ie, condyloma acuminata). Infection is most prevalent in children, adolescents, and young adults and is usually acquired through **direct contact**. Immunosuppressed patients (eg, HIV infection) are at increased risk and often develop numerous, large lesions.

Although the HPV family is associated with an increased risk for mucosal squamous cell carcinoma (eg, cervical cancer), this is primarily related to high-risk HPV types (eg, 16, 18); most cutaneous warts are due to low-risk types (eg, 2, 4), and malignant transformation is rare.

**(Choice A)** **Coxsackievirus** is the most common etiologic agent in hand-foot-and-mouth disease, which is characterized by low-grade fever and vesicles/ulcers on the oral mucosa and skin (especially hands and feet). Chronic papules are more consistent with cutaneous warts.

**(Choice B)** **Herpes simplex virus** causes herpetic whitlow, which presents acutely with a prodrome of



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(Choice B) Herpes simplex virus causes herpetic whitlow, which presents acutely with a prodrome of



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(Choice B) Herpes simplex virus causes herpetic whitlow, which presents acutely with a prodrome of



characterized by low-grade fever and vesicles/ulcers on the oral mucosa and skin (especially hands and feet). Chronic papules are more consistent with cutaneous warts.

**(Choice B)** *Herpes simplex virus* causes herpetic whitlow, which presents acutely with a prodrome of burning/tingling followed by single or multiple vesicles on an erythematous base.

**(Choice D)** Disseminated gonococcal infection causes a pustular or bullous rash, which commonly involves both the extremities and torso. It is typically associated with tenosynovitis and migratory polyarthralgia.

**(Choice E)** *Molluscum contagiosum* is caused by a pox virus. Although it commonly presents as small papules, the lesions are smooth, pearly, and umbilicated, unlike the rough, dry lesions in this patient.

**(Choice F)** Condyloma lata is a manifestation of secondary syphilis, caused by *Treponema pallidum*. Although it may present as verruciform lesions, it is often associated with fever and lymphadenopathy and is most common on the oral mucosa or genital area near the site of primary infection.

### Educational objective:

Cutaneous warts are caused by human papillomavirus (HPV) and typically present as skin-colored papules with a dry, whitish surface. HPV is usually transmitted by direct contact.

### References





characterized by low-grade fever and vesicles/ulcers on the oral mucosa and skin (especially hands and

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characterized by low-grade fever and vesicles/ulcers on the oral mucosa and skin (especially hands and

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A 24-year-old woman comes to the office due to worsening acne. Over the past 3 months, the patient has had frequent breakouts on the shoulders and upper back. She had acne on her face during puberty, which cleared spontaneously after several years, but has never before had symptoms on her trunk. The patient has no other medical conditions, and her only medication is a combination oral contraceptive. She has been training for a half-marathon for the past 4 months and has lost 6.8 kg (15 lb) during this period. She does not use tobacco, alcohol, or illicit drugs, and she relocated from California to Wisconsin for work a year ago. Vital signs are within normal limits. Physical examination shows acneiform eruptions on the shoulders and mid-back. Which of the following is most likely contributing to worsening of this patient's acne?

- ☐ A. Exposure to colder temperatures
- ☐ B. Exposure to contaminated water
- ☐ C. Rapid loss of body weight
- ☐ D. Use of hormonal contraceptive
- ☐ E. Use of tight-fitting sports clothing



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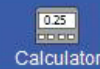
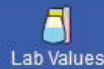




had frequent breakouts on the shoulders and upper back. She had acne on her face during puberty, which cleared spontaneously after several years, but has never before had symptoms on her trunk. The patient has no other medical conditions, and her only medication is a combination oral contraceptive. She has been training for a half-marathon for the past 4 months and has lost 6.8 kg (15 lb) during this period. She does not use tobacco, alcohol, or illicit drugs, and she relocated from California to Wisconsin for work a year ago. Vital signs are within normal limits. Physical examination shows acneiform eruptions on the shoulders and mid-back. Which of the following is most likely contributing to worsening of this patient's acne?

- ☐ A. Exposure to colder temperatures (2%)
- ☐ B. Exposure to contaminated water (1%)
- ☐ C. Rapid loss of body weight (16%)
- ☐ D. Use of hormonal contraceptive (37%)
- ☒ E. Use of tight-fitting sports clothing (42%)





### Acne vulgaris

#### Clinical features

- Comedonal acne: closed or open comedones on forehead, nose & chin
- Inflammatory acne: small, erythematous papules & pustules
- Nodular acne: large, painful nodules; sinus tracts & scarring

#### Pathogenesis

- Hyperkeratinization & obstruction of pilosebaceous follicle
- Sebaceous gland enlargement & increased sebum production
- Metabolism of sebaceous lipids by *Cutibacterium acnes* & release of inflammatory fatty acids
- Follicular inflammation & rupture

#### Risk factors

- Increased circulating androgens (eg, puberty, polycystic ovary syndrome)
- Mechanical trauma/friction (eg, excessive scrubbing, tight clothing)
- Comedogenic oil-based skin & hair products

**Acne vulgaris** is a disorder of the **pilosebaceous follicle**. Hyperkeratinization and obstruction of the follicle in combination with glandular enlargement and increased sebum production provides an optimal





**Acne vulgaris** is a disorder of the **pilosebaceous follicle**. Hyperkeratinization and obstruction of the follicle in combination with glandular enlargement and increased sebum production provides an optimal environment for *Cutibacterium (Propionibacterium) acnes*. This organism metabolizes sebaceous lipids, releasing inflammatory factors that lead to follicular and perifollicular inflammation. Acne is most common in areas with a high concentration of sebaceous follicles, including the face, back, chest, and upper arms.

**Androgens** stimulate production of sebum, and increased androgen levels (eg, puberty, polycystic ovary syndrome) increase the incidence of acne. Obstruction of the glands, such as by **oil-based hair products** (pomade acne), also promotes acne. In addition, **mechanical irritation** can promote acne by increasing glandular occlusion and disruption of follicles (acne mechanica). **Sports participation**, as in this patient, frequently triggers acne due to the use of tight-fitting clothing (eg, sports bras) and protective gear (eg, helmets).

**(Choice A)** High ambient temperatures can worsen acne, leading to formation of painful nodules on the trunk (tropical acne). Colder temperatures are not associated with acne.

**(Choice B)** Exposure to water contaminated with *Pseudomonas aeruginosa* can cause erythematous papules and pustules around hair follicles (hot-tub folliculitis). This condition begins acutely, resolves spontaneously within 1-2 weeks, and typically involves the skin under a bathing suit (eg, buttocks) or on the







**(Choice B)** Exposure to water contaminated with *Pseudomonas aeruginosa* can cause erythematous papules and pustules around hair follicles (hot-tub folliculitis). This condition begins acutely, resolves spontaneously within 1-2 weeks, and typically involves the skin under a bathing suit (eg, buttocks) or on the extremities.

**(Choice C)** Obesity is associated with an increased risk of acne, but weight loss generally does not worsen acne.

**(Choice D)** Typical oral contraceptives do not promote acne. Rather, many commonly used contraceptives can reduce acne due to decreased synthesis of androgens.

### Educational objective:

Risk factors for acne include increased androgen levels; obstruction of pilosebaceous glands by oil-based hair products; and mechanical irritation of skin follicles. Sports participation frequently triggers acne due to the use of tight-fitting clothing and protective gear.

Pathology

Dermatology

Acne vulgaris

Subject

System

Topic

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A 28-year-old man comes to the office with bilateral skin lesions over the posterior surface of the elbows. The lesions are itchy at times; topical moisturizers have reduced the itching, but the lesions have remained. The patient has no chronic medical problems and takes no medications. Biopsy of the lesions demonstrates hyperkeratosis, parakeratosis, dilated capillaries in the dermal papillae, and foci of neutrophils in the superficial epidermis. Which of the following is the most likely diagnosis?

- ☐ A. Atopic dermatitis
- ☐ B. Dermatitis herpetiformis
- ☐ C. Erythema nodosum
- ☐ D. Psoriasis
- ☐ E. Urticaria

Submit





A 28-year-old man comes to the office with bilateral skin lesions over the posterior surface of the elbows. The lesions are itchy at times; topical moisturizers have reduced the itching, but the lesions have remained. The patient has no chronic medical problems and takes no medications. Biopsy of the lesions demonstrates hyperkeratosis, parakeratosis, dilated capillaries in the dermal papillae, and foci of neutrophils in the superficial epidermis. Which of the following is the most likely diagnosis?

- ☐ A. Atopic dermatitis (5%)
- ☐ B. Dermatitis herpetiformis (7%)
- ☐ C. Erythema nodosum (0%)
- ☒ D. Psoriasis (85%)
- ☐ E. Urticaria (1%)

Correct



85%

Answered correctly



33 secs

Time Spent



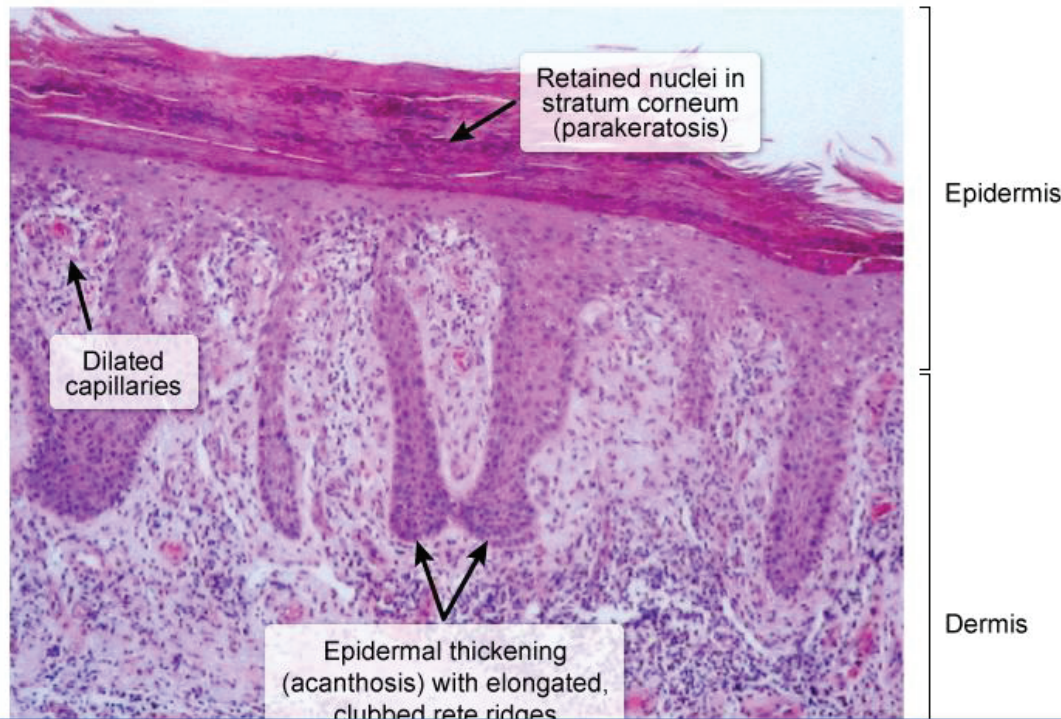
02/22/2021

Last Updated





## Psoriasis





**Psoriasis** is a common chronic inflammatory skin disorder that presents with scaly, erythematous plaques, typically on the extensor surfaces of the elbows and knees. In predisposed individuals, disruption of the epithelial barrier leads to activation of antigen-presenting dendritic cells and subsequently to a self-reinforcing inflammatory cascade characterized by recruitment and activation of T helper cells and **proliferation of keratinocytes**.

Histopathologically, psoriasis is characterized by:

- **Hyperkeratosis** (thickening of the stratum corneum) and confluent parakeratosis (retention of nuclei in the stratum corneum) produces the characteristic silvery scale on gross examination
- **Epidermal hyperplasia** (acanthosis) with elongated rete ridges correspond to the typical erythematous plaques
- **Neutrophilic foci** in the stratum corneum and epidermis, which may coalesce to form microabscesses (Munro microabscesses)

In addition, the epidermal cell layer superficial to the dermal papillae may be thinned and contain **dilated blood vessels**, which leads to **pinpoint bleeding** when the scale is removed from the plaque (Auspitz sign).

(Choice A) Chronic atopic dermatitis can produce plaques characterized by hyperkeratosis and





**(Choice A)** Chronic atopic dermatitis can produce plaques characterized by hyperkeratosis and acanthosis, often with a lymphocytic or eosinophilic infiltrate. However, adults most commonly develop lesions on flexural surfaces (eg, anterior elbows), and most patients have a history of other atopic disorders (eg, asthma, allergic rhinitis) beginning in childhood.

**(Choice B)** Dermatitis herpetiformis presents with erythematous, pruritic papules, vesicles, and bullae symmetrically on the elbows, knees, upper back, and buttocks. It is strongly associated with celiac disease, and histopathology shows microabscesses at the dermal papillary tips, which coalesce to form subepidermal blisters.

**(Choice C)** Erythema nodosum is characterized by painful, red nodules on the shins and often represents an inflammatory response to medications (eg, oral contraceptives), infections, inflammatory bowel disease, or sarcoidosis. Histopathology is variable but typically shows a septal panniculitis with a mixed cellular infiltrate.

**(Choice E)** Urticaria ("hives") is a transient dermatologic disorder that is caused by antigen-induced degranulation of focal mast cells through IgE antibody sensitization. This degranulation causes microvasculature hyperpermeability and the formation of wheals that typically surface and resolve within hours.







**(Choice C)** Erythema nodosum is characterized by painful, red nodules on the shins and often represents an inflammatory response to medications (eg, oral contraceptives), infections, inflammatory bowel disease, or sarcoidosis. Histopathology is variable but typically shows a septal panniculitis with a mixed cellular infiltrate.

**(Choice E)** Urticaria ("hives") is a transient dermatologic disorder that is caused by antigen-induced degranulation of focal mast cells through IgE antibody sensitization. This degranulation causes microvasculature hyperpermeability and the formation of wheals that typically surface and resolve within hours.

### Educational objective:

Psoriasis is characterized by hyperkeratosis and confluent parakeratosis of the stratum corneum, and epidermal hyperplasia (acanthosis) with elongated rete ridges. Neutrophilic foci in the stratum corneum and epidermis may coalesce to form microabscesses (Munro microabscesses).

Pathology

Dermatology

Psoriasis

Subject

System

Topic

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A 2-year-old boy is brought to the office by his mother due to a rash that started 3 days ago. A similar red, itchy rash on the cheeks, trunk, and arms has occurred intermittently since infancy. The mother thought that the rashes were related to the consumption of certain foods, but elimination of cow's milk and fruits did not improve the rash. The patient has had a few upper respiratory infections but no major illnesses. Vaccinations are up to date, and he takes no medications. He attends a day care facility. Vital signs are within normal limits. The rash on the patient's back is shown in the [exhibit](#). Similar findings are observed on the cheeks and proximal upper extremities. The diaper area is clear, and no mucosal lesions are present. This patient's condition is often associated with the development of which of the following disorders?

- ☐ A. Celiac disease
- ☐ B. Extrinsic asthma
- ☐ C. Langerhans cell histiocytosis
- ☐ D. Psoriatic arthritis
- ☐ E. Ulcerative colitis



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Itchy rash on the cheeks, trunk, and arms has occurred intermittently since infancy. The mother thought that the rashes were related to the consumption of certain foods, but elimination of cow's milk and fruits did not improve the rash. The patient has had a few upper respiratory infections but no major illnesses. Vaccinations are up to date, and he takes no medications. He attends a day care facility. Vital signs are within normal limits. The rash on the patient's back is shown in the [exhibit](#). Similar findings are observed on the cheeks and proximal upper extremities. The diaper area is clear, and no mucosal lesions are present. This patient's condition is often associated with the development of which of the following disorders?

- ☐ A. Celiac disease (23%)
- ☒ B. Extrinsic asthma (54%)
- ☐ C. Langerhans cell histiocytosis (12%)
- ☐ D. Psoriatic arthritis (8%)
- ☐ E. Ulcerative colitis (1%)



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Lab Values



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Calculator



Reverse Color



Text Zoom



Settings

### Atopic dermatitis

#### Pathogenesis

- Mutations of filaggrin and other epidermal barrier proteins
- Disrupted skin barrier increases antigen exposure and hypersensitivity
- Associated with asthma & allergic rhinitis

#### Clinical findings

- Intense pruritus
- Infants: red, crusted lesions involving extensor surfaces & face
- Children & adults: flexural eczema & lichenification

#### Laboratory findings

- High serum IgE
- Eosinophilia

**Atopic dermatitis** (AD), or **eczema**, is a **chronic** inflammatory skin disorder common in children. The disease typically occurs at age <5, with many patients developing symptoms in infancy. AD typically presents in infants and young children as erythematous papules and plaques involving the face, scalp, trunk, and extensor surfaces. The diaper area is usually spared. In older children and adults, it often manifests as **lichenification** in a flexural distribution (eg, neck, wrists, antecubital and popliteal fossae).

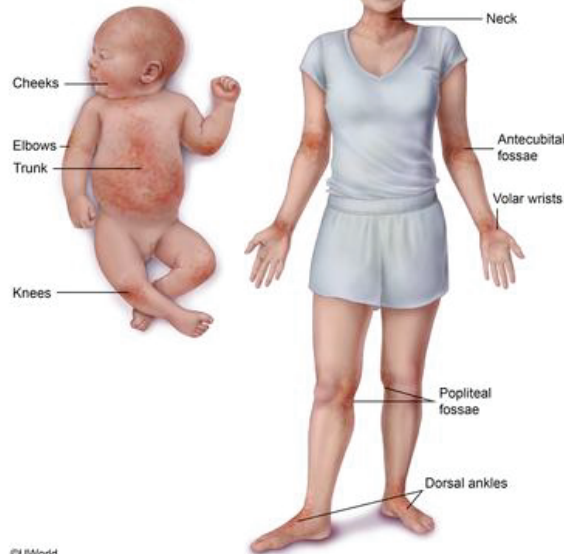


## Exhibit Display

## Atopic dermatitis distribution by age

Child or adult: flexor surfaces

Infant: extensor surfaces



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### Exhibit Display



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Calculator

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Text Zoom

Settings

presents in infants and young children as erythematous papules and plaques involving the face, scalp, trunk, and extensor surfaces. The diaper area is usually spared. In older children and adults, it often manifests as **lichenification** in a flexural distribution (eg, neck, wrists, antecubital and popliteal fossae). Eczema has a chronic course marked by exacerbations and remissions, and its severity tends to lessen with age. Intense **pruritus** is a hallmark of AD.

AD can be associated with mutations affecting epidermal barrier proteins such as filaggrin, resulting in **impairment of the skin's barrier function**. This increases immunologic exposure to environmental allergens and microbial antigens, leading to immune hypersensitivity. Affected patients usually have high serum IgE levels and peripheral eosinophilia. Children with AD often have a **family history** of atopy and are at risk of developing other atopic diseases, such as **allergic rhinitis** and **asthma (allergic triad)**. The risk of developing an additional atopic disease may be inversely related to the age of eczema onset.

**(Choice A)** Celiac disease is associated with **dermatitis herpetiformis**, which presents with pruritic vesicles and plaques on the buttocks and extensor surfaces of the extremities. In addition, this skin disorder is extremely uncommon in children.

**(Choice C)** Langerhans cell histiocytosis is a dendritic cell disorder that can present in infancy or early childhood with a severe, refractory, erythematous or ulcerative rash on the scalp, trunk, or groin. This patient's rash flares and resolves without intervention.



presents in infants and young children as erythematous papules and plaques involving the face, scalp,

Exhibit Display



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patient's rash flares and resolves without intervention.





and plaques on the buttocks and extensor surfaces of the extremities. In addition, this skin disorder is extremely uncommon in children.

**(Choice C)** Langerhans cell histiocytosis is a dendritic cell disorder that can present in infancy or early childhood with a severe, refractory, erythematous or ulcerative rash on the scalp, trunk, or groin. This patient's rash flares and resolves without intervention.

**(Choice D)** Psoriatic arthritis is associated with [psoriasis](#). Manifestations of psoriasis include erythematous, well-demarcated papules and plaques with a silvery scale, which are not seen in this patient.

**(Choice E)** Ulcerative colitis, a type of inflammatory bowel disease, can be associated with dermatologic manifestations, such as [pyoderma gangrenosum](#) (ulcerative rash) or [erythema nodosum](#) (painful raised red nodules). Both are uncommon in children, and neither is seen in this case.

### Educational objective:

Atopic dermatitis (eczema) is a common, chronic inflammatory disorder caused by impairment of the skin's barrier function. Eczema presents with pruritus and erythematous papules and plaques and is associated with other atopic diseases, such as allergic rhinitis and asthma.

### References

- [Advances in atopic dermatitis](#).



and plaques on the buttocks and extensor surfaces of the extremities. In addition, this skin disorder is

Exhibit Display



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and plaques on the buttocks and extensor surfaces of the extremities. In addition, this skin disorder is

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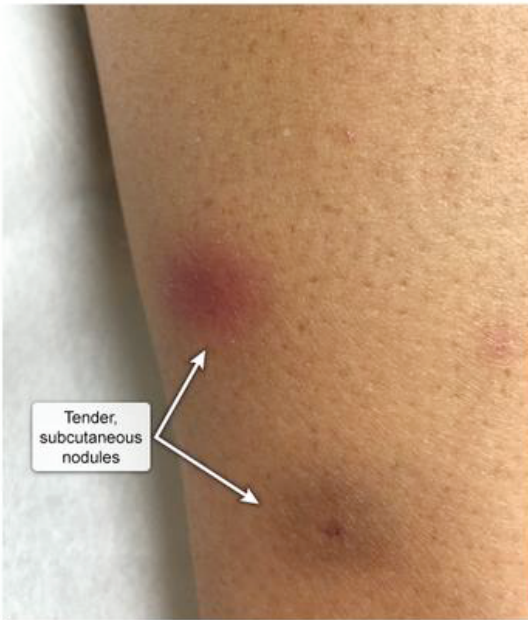
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and plaques on the buttocks and extensor surfaces of the extremities. In addition, this skin disorder is

Exhibit Display

Erythema nodosum



Tender,  
subcutaneous  
nodules

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A 34-year-old woman comes to the office due to skin changes. Blotches of skin on her arms appear to be of a different color, and she also has a tingling sensation in her hands. These symptoms have developed over the past several months. The patient has no other past medical history. She is a political refugee from East Africa. On examination, there are patchy areas of skin anesthesia and hypopigmentation on her upper extremities. Nerve biopsy evaluated under light microscopy shows many organisms invading Schwann cells. HIV testing is negative. Which of the following organisms is the most likely cause of this patient's condition?

- ☐ A. *Borrelia burgdorferi*
- ☐ B. *Campylobacter fetus*
- ☐ C. *Corynebacterium diphtheriae*
- ☐ D. *Mycobacterium leprae*
- ☐ E. *Treponema pallidum*

**Submit**



A 34-year-old woman comes to the office due to skin changes. Blotches of skin on her arms appear to be of a different color, and she also has a tingling sensation in her hands. These symptoms have developed over the past several months. The patient has no other past medical history. She is a political refugee from East Africa. On examination, there are patchy areas of skin anesthesia and hypopigmentation on her upper extremities. Nerve biopsy evaluated under light microscopy shows many organisms invading Schwann cells. HIV testing is negative. Which of the following organisms is the most likely cause of this patient's condition?

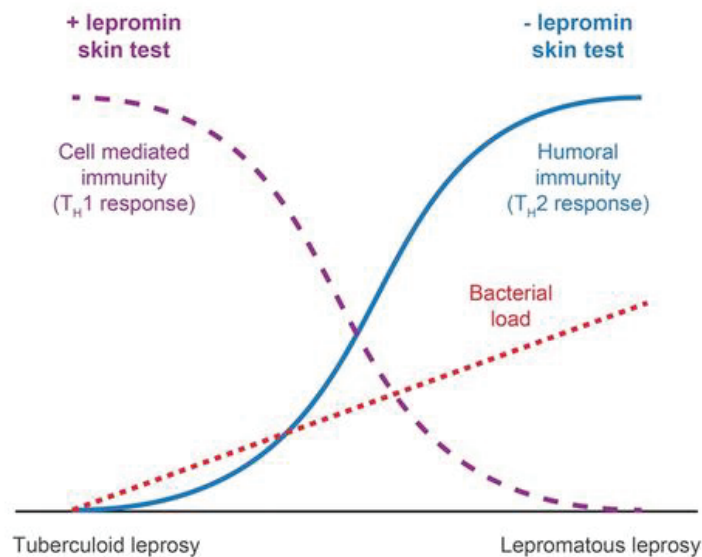
- ☐ A. *Borrelia burgdorferi* (2%)
- ☐ B. *Campylobacter fetus* (6%)
- ☐ C. *Corynebacterium diphtheriae* (1%)
- ☒ D. *Mycobacterium leprae* (84%)
- ☐ E. *Treponema pallidum* (4%)





## Exhibit Display

## Immune response in leprosy





**Leprosy** (Hansen disease), a deforming infection primarily of the **skin** and **nerves**, is caused by *Mycobacterium leprae*. Transmission is promoted in unhygienic conditions and likely occurs through the respiratory route, with some organisms being transmitted through prolonged direct skin-to-skin contact. Infection has also been associated with **armadillo** contact in the southwestern United States. The range of clinical manifestations depends on the strength of the **cell-mediated immune** (CMI) response.

- **Tuberculoid leprosy** (TT) (seen in this patient) is the least severe form and is often self-limited. Mycobacterial infection is limited by an **intact CMI** response (**Th1**-mediated). Mild skin plaques develop and are associated with hypopigmentation, hair follicle loss, and focally decreased sensation.
- **Lepromatous leprosy** (LL), the most severe form, occurs in patients with a **weak CMI** response (Th2-mediated). Macrophage signaling to kill *M leprae* is limited, leading to mycobacterial dissemination. Manifestations include diffuse skin thickening, plaque-like hypopigmentation (often with hair loss), leonine facies, paresis, regional anesthesia, testicular destruction, and blindness.

*M leprae* grows best at temperatures below core body temperature, partially explaining why leprosy manifests in the skin, superficial nerves (eg, Schwann cells in this patient), eyes, and testes. Intermediate features between TT and LL are often seen.





**(Choice A)** *Borrelia burgdorferi* causes Lyme disease. Symptoms include a characteristic skin rash (erythema chronicum migrans) with fever and malaise. Systemic disease can progress to cause arthritis, facial palsy, or cardiac involvement (eg, conduction abnormalities). Prolonged untreated disease can lead to central nervous system involvement.

**(Choice B)** *Campylobacter fetus*, a gram-negative rod, causes mild enteritis in immunocompetent patients and mild systemic bacteremic illness in immunocompromised patients.

**(Choice C)** *Corynebacterium diphtheriae* is a gram-positive rod that causes diphtheria, a primarily toxin-mediated lower respiratory tract infection that is sometimes complicated by polyneuritis and myocarditis.

**(Choice E)** *Treponema pallidum* causes syphilis. Primary syphilis manifests as a painless chancre at the inoculation site. Secondary syphilis results in erythematous macules over the entire body (including the palms and soles) and condyloma lata formation. Tertiary syphilis results in skin and bone gummas and ascending aortitis.

### Educational objective:

The severity of leprosy, a systemic illness caused by *Mycobacterium leprae*, depends on the strength of the cell-mediated immune (CMI) response, with tuberculoid leprosy representing the milder form (intact Th1





lead to central nervous system involvement.

**(Choice B)** *Campylobacter fetus*, a gram-negative rod, causes mild enteritis in immunocompetent patients and mild systemic bacteremic illness in immunocompromised patients.

**(Choice C)** *Corynebacterium diphtheriae* is a gram-positive rod that causes diphtheria, a primarily toxin-mediated lower respiratory tract infection that is sometimes complicated by polyneuritis and myocarditis.

**(Choice E)** *Treponema pallidum* causes syphilis. Primary syphilis manifests as a painless chancre at the inoculation site. Secondary syphilis results in erythematous macules over the entire body (including the palms and soles) and condyloma lata formation. Tertiary syphilis results in skin and bone gummas and ascending aortitis.

### Educational objective:

The severity of leprosy, a systemic illness caused by *Mycobacterium leprae*, depends on the strength of the cell-mediated immune (CMI) response, with tuberculoid leprosy representing the milder form (intact Th1 CMI response) and lepromatous leprosy, the more severe form (weak CMI response).

Microbiology	Dermatology	Leprosy
Subject	System	Topic

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A 22-year-old woman comes to the office due to several years of persistent facial blemishing that has failed to respond to over-the-counter treatment. The patient has no other medical conditions. She does not use tobacco, alcohol, or illicit drugs. Skin examination findings are shown in the image below:





Which of the following most likely contributed to the pathogenesis of this patient's skin condition?

- ☐ A. Androgen-induced involution of sebaceous glands
- ☐ B. Bacterial degradation of apocrine gland secretions
- ☐ C. Estrogen-stimulated secretory function of sebaceous glands
- ☐ D. Increased desquamation of follicular epithelial cells
- ☐ E. Proliferation of lipid-utilizing bacteria within pilosebaceous follicles

Submit







Which of the following most likely contributed to the pathogenesis of this patient's skin condition?

- ☐ A. Androgen-induced involution of sebaceous glands (19%)
- ☐ B. Bacterial degradation of apocrine gland secretions (4%)
- ☐ C. Estrogen-stimulated secretory function of sebaceous glands (9%)
- ☐ D. Increased desquamation of follicular epithelial cells (3%)
- ☒ E. Proliferation of lipid-utilizing bacteria within pilosebaceous follicles (63%)

Correct

63%



01 min, 41 secs



11/09/2020

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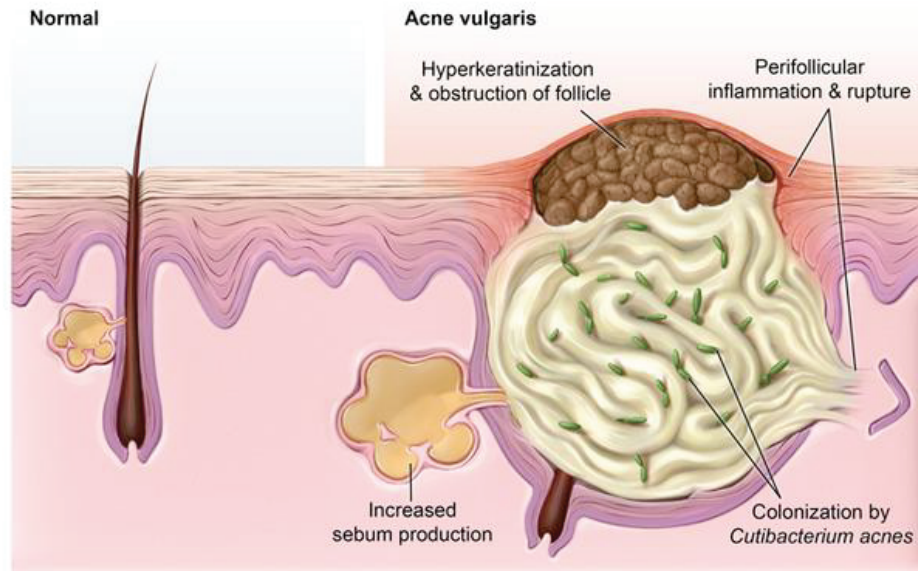
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## Exhibit Display

## Pathogenesis of acne



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This patient's red papules and pustules on the face are consistent with **inflammatory acne**. The pathogenesis of acne involves the following:

- **Hyperkeratinization** due to abnormal epithelial growth and differentiation of corneocytes leads to keratin plug formation in the pilosebaceous follicles. These blocked follicles are referred to as comedones (ie, **whiteheads** and **blackheads**).
- In response to **androgen stimulation** (eg, during pubertal adrenarche), **sebaceous glands** enlarge (not involute) and increase production of sebum, a lipid-rich substance that facilitates obstruction of pilosebaceous follicles (**Choice A**).
- **Cutibacterium acnes**, an anaerobic bacteria that relies on sebum as a nutrient source, proliferates in occluded follicles, triggering an **inflammatory response** that results in the red papules and pustules characteristic of **nodulocystic acne**.

**(Choice B)** Bacterial metabolism of apocrine secretions contributes to body odor. Bromhidrosis is a condition characterized by excessive and offensive body odor.

**(Choice C)** Estrogen has antiandrogenic effects and inhibits sebum production. For this reason, estrogen-containing oral contraceptives help to improve inflammatory acne.





## Exhibit Display



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Tutorial



Lab Values



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### Exhibit Display



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Exhibit Display



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**(Choice B)** Bacterial metabolism of apocrine secretions contributes to body odor. Bromhidrosis is a condition characterized by excessive and offensive body odor.

**(Choice C)** Estrogen has antiandrogenic effects and inhibits sebum production. For this reason, estrogen-containing oral contraceptives help to improve inflammatory acne.

**(Choice D)** As epithelial stem cells undergo mitosis in the basal layers of the epidermis, newer cells form and undergo differentiation as they migrate toward the surface, replacing epithelial cells that desquamate. Increased epithelial mitosis and desquamation (ie, topical retinoids) helps extrude debris from comedones, limiting acne formation.

### Educational objective:

Acne is characterized by the obstruction of pilosebaceous follicles (ie, comedones) due to hyperkeratinization and excessive sebum accumulation. Androgens stimulate production of sebum, which serves as a nutrient source for *Cutibacterium acnes*. Within the follicles, *C acnes* proliferation triggers an inflammatory response, resulting in formation of red papules and pustules.

Pathophysiology

Dermatology

Acne vulgaris

Subject

System

Topic





A 27-year-old man comes to the office for evaluation of a rash on both knees. The patient first noticed the rash 2 months ago. He has no other medical conditions and takes no medications. The patient smokes a half pack of cigarettes daily. Vital signs are normal. His knee is shown in the image below:





Mark



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Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



Removal of the scale results in small bleeding points. As part of the treatment regimen, a topical vitamin D analog is prescribed. This medication is most likely to improve this patient's condition via which of the following mechanisms?

- ☐ A. Decreased activity of tyrosinase enzyme
- ☐ B. Decreased levels of irritating fatty acids
- ☐ C. Increased production of dermal cytokines
- ☒ D. Inhibition of dermal cyclooxygenase
- ☐ E. Inhibition of keratinocyte proliferation

Submit

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Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



Removal of the scale results in small bleeding points. As part of the treatment regimen, a topical vitamin D analog is prescribed. This medication is most likely to improve this patient's condition via which of the following mechanisms?

- ☐ A. Decreased activity of tyrosinase enzyme (3%)
- ☐ B. Decreased levels of irritating fatty acids (3%)
- ☐ C. Increased production of dermal cytokines (3%)
- ☐ D. Inhibition of dermal cyclooxygenase (4%)
- ☒ E. Inhibition of keratinocyte proliferation (84%)



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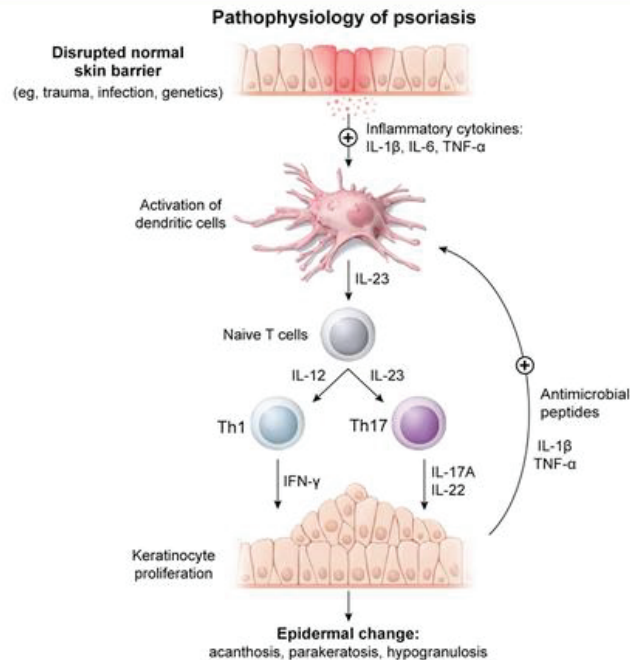


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### Exhibit Display



IFN = interferon; TNF = tumor necrosis factor.

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peptides



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IFN = interferon; TNF = tumor necrosis factor.

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This patient has **psoriasis**, a common skin disorder characterized by activation of T helper cells and proliferation of keratinocytes. Epidermal hyperplasia (acanthosis) produces **erythematous plaques**, and hyperkeratosis and confluent parakeratosis of the stratum corneum produce the characteristic **scaling**. The epidermal cell layer superficial to the dermal papillae may be thinned and contain dilated blood vessels, which can lead to **pinpoint bleeding** when the scale is removed (Auspitz sign).

**First-line treatment** options for localized psoriasis include topical **corticosteroids** (eg, diflorasone) and **vitamin D analogs** (eg, calcipotriene, calcitriol). Vitamin D analogs activate the vitamin D receptor, a nuclear transcription factor, resulting in **inhibition of T-cell and keratinocyte proliferation** and stimulation of keratinocyte differentiation. Corticosteroids also have anti-inflammatory and antiproliferative properties; their mechanism of action is complementary to vitamin D analogs, and the 2 agents work well in combination.

**(Choice A)** Tyrosinase is the primary enzyme responsible for oxidation of tyrosine, which serves as the rate-limiting step in synthesis of melanin. Tyrosinase inhibitors (eg, hydroquinone) decrease synthesis of melanin and can be used in treatment of hyperpigmentation disorders (eg, melasma).

**(Choice B)** Acne vulgaris is promoted by proinflammatory fatty acid production by *Cutibacterium*



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Feedback



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End Block





**(Choice B)** Acne vulgaris is promoted by proinflammatory fatty acid production by *Cutibacterium* (*Propionibacterium*) *acnes*. Benzoyl peroxide has bacteriostatic properties against *C acnes* and reduces production of these inflammatory fatty acids.

**(Choice C)** Cutaneous warts are the most common manifestation of human papillomavirus infection. Imiquimod is a topical immunomodulator that likely induces local cytokine (eg, interferon-alpha, interleukin-6) production against the virus.

**(Choice D)** Prostaglandin E<sub>2</sub> (which is produced by cyclooxygenase-2) is involved in mediating the tumorigenic effects of ultraviolet light in the skin, promoting the formation of actinic keratosis (AK) and squamous cell carcinoma. Topical diclofenac, a nonsteroidal anti-inflammatory drug that inhibits cyclooxygenase, can be used to treat AK.

### Educational objective:

First-line treatment options for localized psoriasis include high-potency topical corticosteroids and vitamin D analogs. Vitamin D analogs inhibit T-cell and keratinocyte proliferation and stimulate keratinocyte differentiation. Corticosteroids also have anti-inflammatory and antiproliferative properties; their mechanism of action is complementary to the vitamin D analogs.

### References





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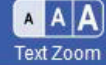
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A 60-year-old woman comes to the physician with 10 days of diffuse itching. A rash began on her hands and quickly spread to involve her wrists, arms, and axillae. She has difficulty sleeping and complains of intense itching in these areas. She works in a day care center and primarily takes care of children age 2-5. The patient has no other medical conditions and takes no chronic medications. Vital signs are normal. Her BMI is 24 kg/m<sup>2</sup>. Skin examination shows small erythematous papules on the palms with excoriations, scattered vesicles, and pustules on the finger webs, palms, and wrist creases, as seen in the image below. She has similar lesions in her axillary skin folds bilaterally. The remainder of the examination is within normal limits.



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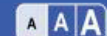
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Which of the following is the most likely finding on skin sampling of this patient's lesions?

- ☐ A. Budding yeast
- ☐ B. Molluscum bodies
- ☐ C. Multinucleated giant cells
- ☐ D. Necrotic keratinocytes in the epidermis
- ☐ E. *Sarcoptes scabiei* mite and eggs

Submit



Which of the following is the most likely finding on skin sampling of this patient's lesions?

- ☐ A. Budding yeast (2%)
- ☐ B. Molluscum bodies (6%)
- ☐ C. Multinucleated giant cells (7%)
- ☐ D. Necrotic keratinocytes in the epidermis (4%)
- ☒ E. *Sarcoptes scabiei* mite and eggs (79%)

Correct

79%

01 min, 24 secs

11/11/2020

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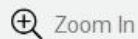
## Exhibit Display

## Scabies

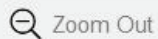


*Sarcoptes  
scabiei* mite

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End Block





This patient's presentation – rapidly spreading, pruritic rash with erythematous papules and excoriations on the extremities - suggests scabies. **Scabies** is due to infestation by the ***Sarcoptes scabiei*** mite, which burrows into the skin and spreads through direct person-to-person contact. It usually presents with an **intensely pruritic rash** in the **flexor surfaces of the wrist**, lateral surfaces of the **fingers**, and the finger webs. The pruritus is often **worse at night** and is due to a delayed type IV hypersensitivity reaction to the mite, mite feces, and mite eggs. Scabies can also involve other parts of the body (eg, elbow extensor surfaces, **axillary folds**).

Skin examination usually shows **excoriations** with small, crusted, red papules scattered around the region. Patients can also develop small vesicles, pustules, or wheals. **Linear burrows** are the most specific finding in scabies, although they are often obscured by excoriations. Diagnosis is confirmed by skin scrapings from excoriated lesions that show **mites, ova, and feces** under light microscopy.

**(Choice A)** Budding yeast indicates *Candida* infection, which most commonly occurs in skin folds with increased moisture and friction. Risk factors include obesity or conditions that interfere with the immune system (eg, diabetes, systemic steroids). *Candida intertrigo* usually presents with erythematous plaques and erosions with satellite papules or pustules that can occur in the axillae, genital areas, and other skin folds.





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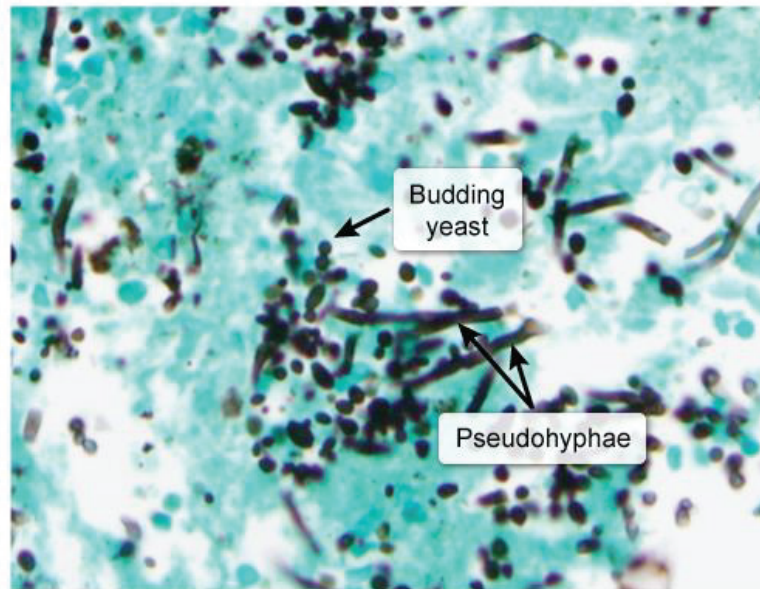
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### Exhibit Display

#### *Candida*



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## Exhibit Display

## Candidal intertrigo (Intertriginous candidiasis)



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**(Choice B)** Molluscum bodies indicate molluscum contagiosum, which is caused by a DNA poxvirus.

Patients can develop single or multiple lesions that are smooth, 2-6 mm wide, whitish or skin-colored, and firm, and appear as pearly papules often with central umbilication. However, molluscum contagiosum does not typically involve the palms and soles.

**(Choice C)** Epidermal multinucleated giant cells are seen with herpes simplex and varicella-zoster virus infections. Herpes simplex typically causes vesicular eruptions involving the perioral or genital regions, while varicella-zoster causes a diffuse vesicular rash (primary infection) or more limited dermatomal involvement (eg, shingles). However, this patient's rash distribution (predominantly palms and axilla) is not characteristic of either virus.

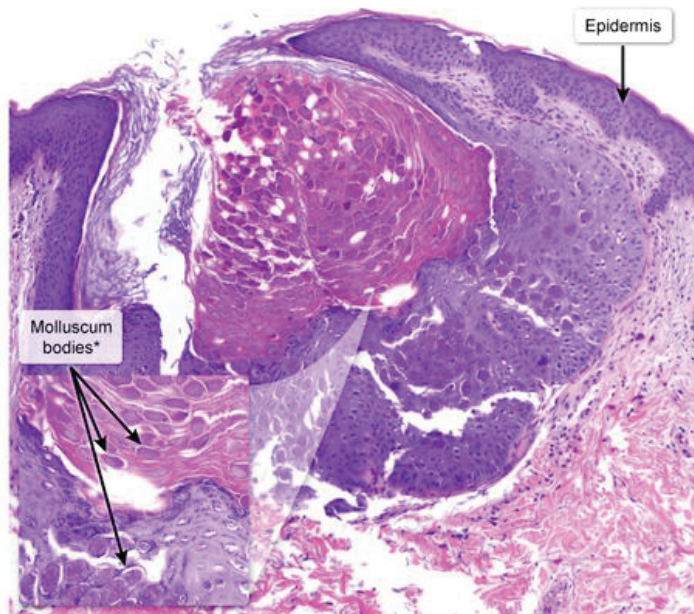
**(Choice D)** Necrotic keratinocytes in the epidermis suggest Stevens-Johnson syndrome, a severe reaction that occurs 1-3 weeks after an infection (eg, cytomegalovirus, *Mycoplasma*) or drug exposure. Patients usually develop high fever, skin pain, mucosal erosions, and skin detachment. However, it typically does not involve the palms and soles. In addition, this patient has no evidence of skin detachment.

**Educational objective:**

Scabies is a highly contagious disease that presents with an intensely pruritic rash (usually worse at night) involving the flexor surfaces of the wrist, lateral surfaces and webs of the fingers, elbow extensor surfaces,

Exhibit Display

Molluscum contagiosum



\*Intracytoplasmic viral inclusions

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## Exhibit Display

## Molluscum contagiosum



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## Exhibit Display

## Shingles



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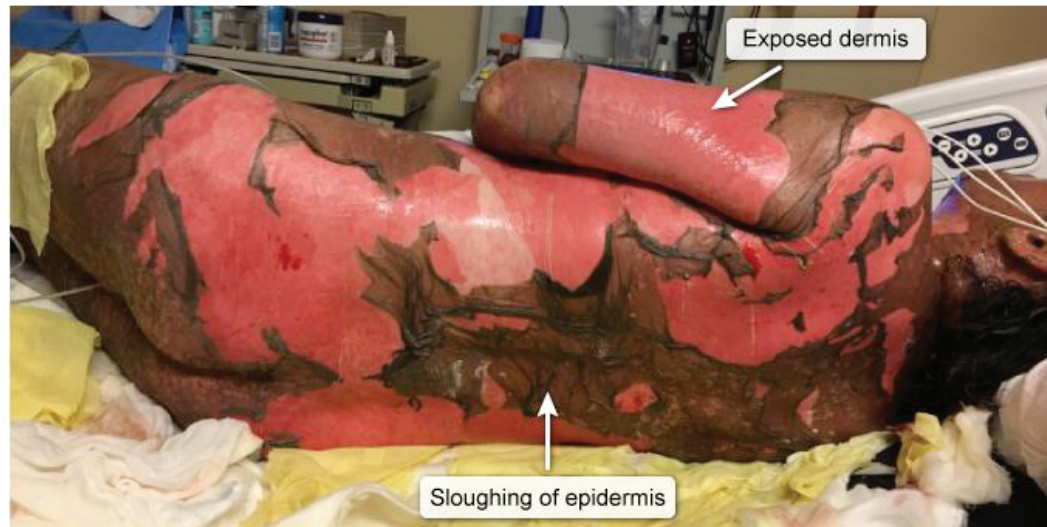
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## Exhibit Display

## Stevens-Johnson syndrome



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**(Choice C)** Epidermal multinucleated giant cells are seen with herpes simplex and varicella-zoster virus infections. Herpes simplex typically causes vesicular eruptions involving the perioral or genital regions, while varicella-zoster causes a diffuse vesicular rash (primary infection) or more limited dermatomal involvement (eg, [shingles](#)). However, this patient's rash distribution (predominantly palms and axilla) is not characteristic of either virus.

**(Choice D)** Necrotic keratinocytes in the epidermis suggest [Stevens-Johnson syndrome](#), a severe reaction that occurs 1-3 weeks after an infection (eg, cytomegalovirus, *Mycoplasma*) or drug exposure. Patients usually develop high fever, skin pain, mucosal erosions, and skin detachment. However, it typically does not involve the palms and soles. In addition, this patient has no evidence of skin detachment.

### Educational objective:

Scabies is a highly contagious disease that presents with an intensely pruritic rash (usually worse at night) involving the flexor surfaces of the wrist, lateral surfaces and webs of the fingers, elbow extensor surfaces, and axillary folds. Patients usually have excoriations with small, crusted, red papules scattered around the affected areas. Diagnosis is confirmed by skin scrapings from excoriated lesions that show mites, ova, and feces under light microscopy.







A 45-year-old woman is brought to the emergency department after a generalized tonic-clonic seizure. She reports no prior history of seizures, but she has noticed right arm weakness over the last week. Her family history is significant for her mother's death from skin cancer. Physical examination shows a skin lesion measuring 13 mm on her back, as shown in the image below.





This lesion most likely originated from which of the following embryologic derivatives?

- ☐ A. Endoderm
- ☐ B. Mesoderm
- ☐ C. Neural crest
- ☐ D. Neuroectoderm
- ☐ E. Surface ectoderm

Submit





This lesion most likely originated from which of the following embryologic derivatives?

- ☐ A. Endoderm (0%)
- ☐ B. Mesoderm (2%)
- ☒ C. Neural crest (71%)
- ☐ D. Neuroectoderm (11%)
- ☐ E. Surface ectoderm (13%)

Correct

71%



23 secs



11/19/2020





### Clinical features of melanoma (ABCDE)

- **A**symmetry: when bisected, the 2 sides are not identical
- **B**order irregularities: uneven edges, pigment fading off
- **C**olor variegation: variable mixtures of brown, tan, black & red
- **D**iameter:  $\geq 6$  mm
- **E**volving: lesion changing in size, shape, or color; new lesion

This patient's family history of skin cancer, the melanocytic lesion seen on skin examination, and her 1-week history of focal neurologic deficit suggest that her seizure results from malignant melanoma metastatic to the central nervous system. Melanoma commonly metastasizes to the brain, gastrointestinal tract, bone, liver, and lungs. It is a malignancy of melanocytes, which are of neural crest origin.

**(Choice A)** The endoderm gives rise to all structures derived from the inner lining of the primitive gut tube. These include the thyroid follicular cells; epithelial surfaces of the trachea, bronchi, and lungs; liver and biliary tree; pancreas; and gastrointestinal and bladder epithelium.

**(Choice B)** The mesoderm gives rise to the dermis as well as most bones, muscles, blood vessels, and visceral tissue.

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**(Choice A)** The endoderm gives rise to all structures derived from the inner lining of the primitive gut tube. These include the thyroid follicular cells; epithelial surfaces of the trachea, bronchi, and lungs; liver and biliary tree; pancreas; and gastrointestinal and bladder epithelium.

**(Choice B)** The mesoderm gives rise to the dermis as well as most bones, muscles, blood vessels, and visceral tissue.

**(Choice D)** The neuroectoderm gives rise to the central nervous system, preganglionic autonomic neurons, retina, and posterior pituitary.

**(Choice E)** The surface ectoderm gives rise to the epidermis and its appendages, mammary glands (modified sweat glands), lens of the eye, and adenohypophysis.

**Educational objective:**

The most common metastatic tumors to the brain are lung cancer, renal cancer, and melanoma. Melanoma is a malignancy of melanocytes, which are embryologically derived from neural crest cells.

**References**

- Incidence of brain metastases in a cohort of patients with carcinoma of the breast, colon, kidney, and lung and melanoma.
- Incidence proportions of brain metastases in patients diagnosed (1973 to 2001) in the Metropolitan

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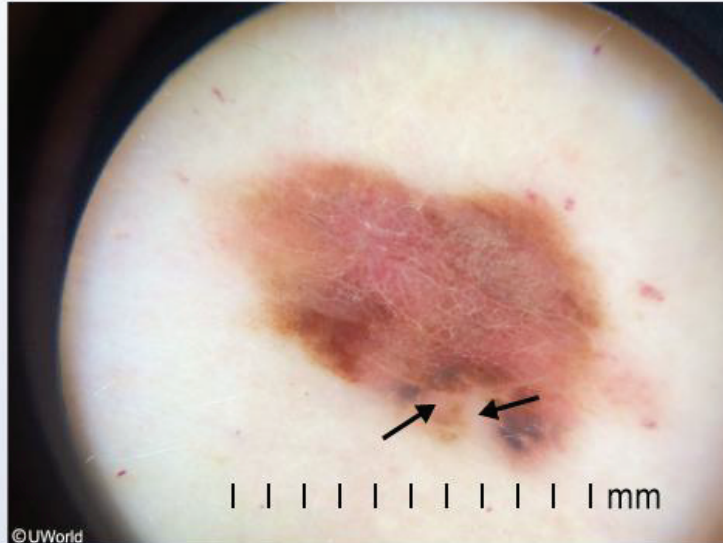
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www.ncbi.nlm.nih.gov/pubmed/12173339

A 50-year-old woman comes to the office for evaluation of a mole on her back. The mole has been present for several years, but her daughter is concerned that it might have grown larger lately. The patient has no other medical conditions but had frequent sunburns during childhood. Dermoscopic examination of the lesion is shown in the image below.



The lesion has multiple color variations, including dark brown, pink, red, and whitish areas. Excisional





The lesion has multiple color variations, including dark brown, pink, red, and whitish areas. Excisional biopsy of the lesion is performed. The whitish areas (arrows) seen on histologic examination most likely represent which of the following underlying processes?

- ☐ A. Intense inflammation
- ☐ B. Melanocyte regression
- ☐ C. Proliferating, neoplastic melanocytes
- ☐ D. Proliferating, nonneoplastic melanocytes
- ☐ E. Vessel ectasia

Submit





The lesion has multiple color variations, including dark brown, pink, red, and whitish areas. Excisional biopsy of the lesion is performed. The whitish areas (arrows) seen on histologic examination most likely represent which of the following underlying processes?

- ☐ A. ~~Intense inflammation~~ (3%)
- ☒ B. Melanocyte regression (43%)
- ☐ C. ~~Proliferating, neoplastic melanocytes~~ (31%)
- ☐ D. ~~Proliferating, nonneoplastic melanocytes~~ (9%)
- ☐ E. Vessel ectasia (10%)

Correct

43%



02 mins, 04 secs



02/21/2021

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This patient who had multiple sunburns as a child has a skin lesion with several classic features of **melanoma**, including **A**symmetry, **B**order irregularity, **C**olor variegation, **D**iameter  $\geq 6$  mm (hash marks), and **E**volution over time.

**Color variegation** is a common feature of melanoma; the different colors represent different areas of activity within the tumor:

- Red areas are due to vessel ectasia (dilation) and local inflammation (**Choices A and E**).
- Brown or black, flared areas along the border are due to advancing, neoplastic melanocytes (**Choice C**).
- White and gray areas appear when **cytotoxic T lymphocytes** recognize tumor antigens (eg, melan-A) and induce apoptosis, leading to malignant **melanocyte regression** (cleared patches).

Melanocyte regression is also a hallmark of treatment response to melanoma immunotherapies, such as the programmed cell death receptor-1 (**PD-1**) **inhibitor** pembrolizumab.

(**Choice D**) This patient's skin findings are characteristic of malignant melanoma. Proliferating nonneoplastic melanocytes do not generally play a role in the development or progression of melanoma.

**Educational objective:**





- Red areas are due to vessel ectasia (dilation) and local inflammation (**Choices A and E**).
- Brown or black, flared areas along the border are due to advancing, neoplastic melanocytes (**Choice C**).
- White and gray areas appear when **cytotoxic T lymphocytes** recognize tumor antigens (eg, melan-A) and induce apoptosis, leading to malignant **melanocyte regression** (cleared patches).

Melanocyte regression is also a hallmark of treatment response to melanoma immunotherapies, such as the programmed cell death receptor-1 (**PD-1**) **inhibitor** pembrolizumab.

**(Choice D)** This patient's skin findings are characteristic of malignant melanoma. Proliferating nonneoplastic melanocytes do not generally play a role in the development or progression of melanoma.

### Educational objective:

Melanoma lesions often have multiple color variations. The different colors represent different activities within the tumor. Whitish/gray areas occur when cytotoxic T cells recognize tumor antigens and destroy malignant cells, leading to melanocyte regression. Red areas arise due to vessel ectasia and local inflammation, whereas brown or black areas are generally due to advancing malignant melanocytes.

Immunology

Dermatology

Melanoma

Subject

System

Topic



A 68-year-old woman comes to the office for evaluation of a skin rash. The patient says that red, painful papules erupted on her right chest 5 days ago and quickly turned into vesicles containing clear fluid. The lesions are now beginning to crust and are less painful. She has never had similar lesions and does not recall coming into contact with a person having a similar illness. Medical history is significant only for well-controlled hypertension. Physical examination shows a grouped vesicular rash involving the right T4 dermatome that is beginning to heal with crusting. The rash does not cross the midline. Lightly touching the skin elicits sharp pain. The remainder of the examination shows no abnormalities. This patient is at greatest risk of developing which of the following complications as a result of her current condition?

- ☐ A. Dissemination of rash to other body areas
- ☐ B. Painful swelling of the large joints
- ☐ C. Persistent pain in the affected region
- ☐ D. Recurrent episodes of gross hematuria
- ☐ E. Sensory loss in "glove and stocking" pattern





A 68-year-old woman comes to the office for evaluation of a skin rash. The patient says that red, painful papules erupted on her right chest 5 days ago and quickly turned into vesicles containing clear fluid. The lesions are now beginning to crust and are less painful. She has never had similar lesions and does not recall coming into contact with a person having a similar illness. Medical history is significant only for well-controlled hypertension. Physical examination shows a grouped vesicular rash involving the right T4 dermatome that is beginning to heal with crusting. The rash does not cross the midline. Lightly touching the skin elicits sharp pain. The remainder of the examination shows no abnormalities. This patient is at greatest risk of developing which of the following complications as a result of her current condition?

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- ☐ A. Dissemination of rash to other body areas (3%)
- ☐ B. Painful swelling of the large joints (3%)
- ☒ C. Persistent pain in the affected region (85%)
- ☐ D. Recurrent episodes of gross hematuria (1%)
- ☐ E. Sensory loss in "glove and stocking" pattern (6%)

Correct

85%



04 mins, 03 secs



09/20/2020

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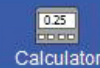
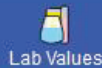
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This patient has a vesicular rash consistent with **herpes zoster** (shingles), which is caused by **reactivation** of latent varicella-zoster virus (VZV) infection. Following the primary infection (**chickenpox**), VZV remains dormant in the **dorsal root ganglia** until emerging decades later. Decreased cell-mediated immunity (eg, older age, immunosuppressive medications, HIV infection) increases the risk of reactivation.

Reactivation of VZV causes hemorrhagic inflammation of the dorsal root ganglion and peripheral nerve. The resulting hypersensitive nerve function presents with **neuropathic pain** in the affected region (herpetic neuralgia), typically described as stabbing, tingling, or burning. Herpetic neuralgia can begin even before the appearance of skin lesions and may persist for up to several months. A minority of patients experience **long-term residual pain**, termed **postherpetic neuralgia**; the risk is greater in older patients (age >70) and those with more severe shingles.

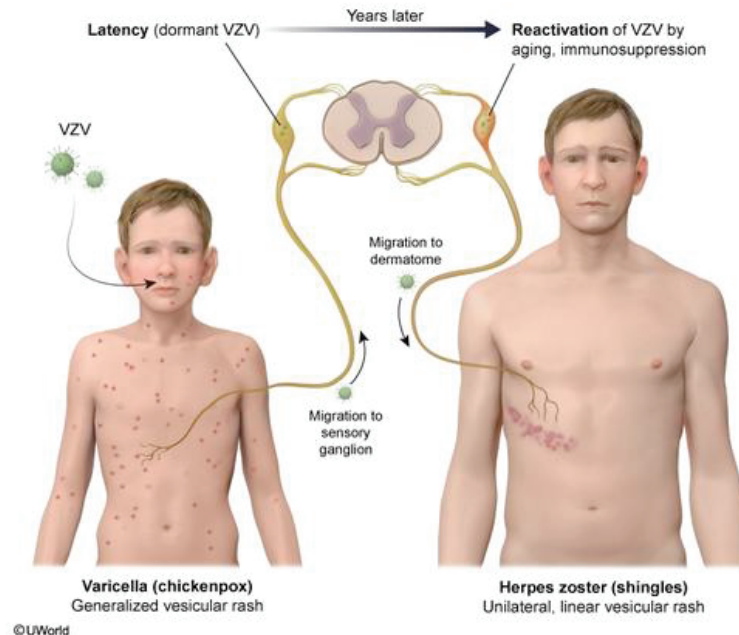
**(Choice A)** Primary VZV infection is characterized by a diffuse vesicular rash (chickenpox), but reactivation is dermatomal. Generalized reactivation or spread to other body areas can occur in immune-compromised patients but is extremely rare in healthy individuals.

**(Choice B)** Reactive arthritis presents with an asymmetric peripheral oligoarthritis, often with extraarticular symptoms (eg, uveitis, conjunctivitis, urethritis). It typically follows bacterial gastrointestinal (eg, *Salmonella*, *Shigella*, *Campylobacter*) or genitourinary (eg, *Chlamydia*) infection.



### Exhibit Display

#### Varicella-zoster virus (VZV) infection



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reactivation is dermatomal. Generalized reactivation or spread to other body areas can occur in immune-compromised patients but is extremely rare in healthy individuals.

**(Choice B)** Reactive arthritis presents with an asymmetric peripheral oligoarthritis, often with extraarticular symptoms (eg, uveitis, conjunctivitis, urethritis). It typically follows bacterial gastrointestinal (eg, *Salmonella*, *Shigella*, *Campylobacter*) or genitourinary (eg, *Chlamydia*) infection.

**(Choice D)** IgA nephropathy produces recurrent glomerulonephritis and typically presents with episodic hematuria. Common triggers include upper respiratory illness, but shingles does not typically exacerbate the condition.

**(Choice E)** Toxic or metabolic nerve injury (eg, diabetic peripheral neuropathy) is typically proportionate to the length of the sensory nerve fibers. Symptoms appear first in the longest nerves, such as those to the feet and hands, causing a "glove and stocking" distribution. However, because reactivation of VZV occurs only in specific sensory ganglia, symptoms have a dermatomal distribution.

**Educational objective:**

A unilateral vesicular rash localized on a single dermatome in an older patient is most likely herpes zoster. Postherpetic neuralgia is the most common neurologic complication of varicella zoster virus infection.





A 34-year-old woman comes to the office due to 3 days of discomfort and swelling in the right axilla. The patient has no known medical problems. She is the local community veterinarian and volunteers as a swim coach at her children's school. She owns a parrot and a hamster. Temperature is 36.9 C (98.4 F). On physical examination, there is an enlarged, tender axillary lymph node on the right, measuring about 3 cm and with slight surrounding erythema but no skin breakdown. There is no other area of lymphadenopathy present. Several scratch marks are seen on the right arm. The organism responsible for the lymphadenopathy is also associated with which of the following conditions?

- ☐ A. Bacillary angiomatosis
- ☐ B. Bladder cancer
- ☐ C. Condylomata acuminata
- ☐ D. Hemolytic uremic syndrome
- ☐ E. Malignant external otitis
- ☐ F. Toxic shock syndrome





patient has no known medical problems. She is the local community veterinarian and volunteers as a swim coach at her children's school. She owns a parrot and a hamster. Temperature is 36.9 C (98.4 F). On physical examination, there is an enlarged, tender axillary lymph node on the right, measuring about 3 cm and with slight surrounding erythema but no skin breakdown. There is no other area of lymphadenopathy present. Several scratch marks are seen on the right arm. The organism responsible for the lymphadenopathy is also associated with which of the following conditions?

- ☒ A. Bacillary angiomatosis (83%)
- ☐ B. Bladder cancer (1%)
- ☐ C. Condylomata acuminata (3%)
- ☐ D. Hemolytic uremic syndrome (3%)
- ☐ E. Malignant external otitis (3%)
- ☒ F. Toxic shock syndrome (4%)

Incorrect

Correct answer

83%

Answered correctly



02 mins, 06 secs

Time spent



12/29/2020

Last updated

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This patient with extensive animal exposure and scratch marks on her arm likely has **cat-scratch disease** (cat-scratch fever), a condition caused by ***Bartonella henselae***. This organism resides in the oral cavity of cats and is transmitted to humans by cat scratches and bites. Typically, a primary inoculation lesion evolves from vesicular to erythematous to papular, followed by the development of **tender regional lymphadenopathy** (often involving a single lymph node) proximal to the lesion. **Axillary** lymphadenopathy is extremely common.

*B. henselae* can also cause **bacillary angiomatosis** (BA) in immunocompromised patients. BA presents with red-purple papular **skin lesions**. These vascular proliferations may also be found within the viscera. BA can be fatal if left untreated.

**(Choice B)** *Schistosoma haematobium*, which can present acutely as swimmer's itch (organism penetration into skin) or Katayama fever (fever, urticaria, angioedema, eosinophilia), can affect the bladder (causing terminal hematuria, fibrosis); chronic infection is a risk factor for bladder cancer.

**(Choice C)** Condylomata acuminata (genital warts) are caused by *Human papillomavirus 6 and 11*. They present as soft, tan, cauliflowerlike masses on the penis, vulva, and perianal areas.

**(Choice D)** Hemolytic uremic syndrome is the triad of microangiopathic hemolytic anemia, thrombocytopenia, and renal insufficiency caused by *Escherichia coli* strain O157:H7.



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thrombocytopenia, and renal insufficiency caused by *Escherichia coli* strain O157:H7





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Settings

(causing terminal hematuria, fibrosis); chronic infection is a risk factor for bladder cancer.

**(Choice C)** Condylomata acuminata (genital warts) are caused by *Human papillomavirus 6* and *11*. They present as soft, tan, cauliflowerlike masses on the penis, vulva, and perianal areas.

**(Choice D)** Hemolytic uremic syndrome is the triad of microangiopathic hemolytic anemia, thrombocytopenia, and renal insufficiency caused by *Escherichia coli* strain O157:H7.

**(Choice E)** *Pseudomonas aeruginosa* can cause malignant otitis externa in individuals using contaminated swimming pools and hot tubs. Pseudomonal hot tub folliculitis typically manifests as a rash rather than lymphadenopathy.

**(Choice F)** Toxic shock syndrome (TSS) is caused by *Staphylococcus aureus*. TSS presents with fever, vomiting, diarrhea, desquamation, and hypotension.

### Educational objective:

*Bartonella henselae* causes cat-scratch disease, bacillary angiomatosis, and culture-negative endocarditis. Cat-scratch disease is characterized by low fever, lymphadenopathy, and a self-limited course.

Microbiology

Dermatology

Bartonella

Subject

System

Topic







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Reverse Color

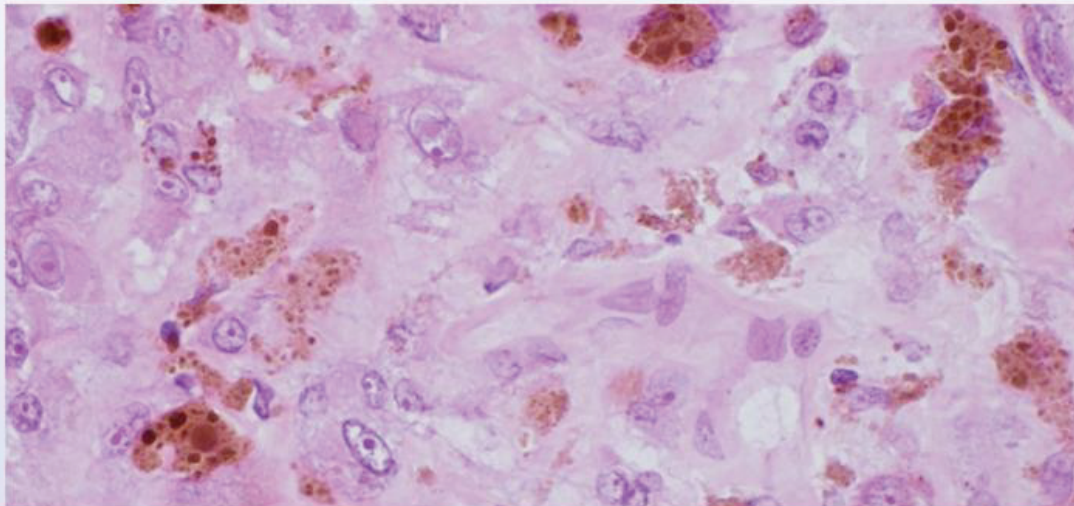


Text Zoom



Settings

A 65-year-old man comes to the office due to 2 months of fatigue and persistent, nonproductive cough. He has a history of coronary artery disease and myocardial infarction. Three years ago, he underwent wide local excision of a melanoma on his posterior neck. The patient has a 50-pack-year smoking history. Vital signs are within normal limits. Chest radiograph reveals multiple lung lesions and hilar lymphadenopathy. Histopathology from one of the biopsied lung lesions is shown below after staining with hematoxylin and eosin.



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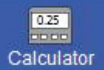
Tutorial



Lab Values



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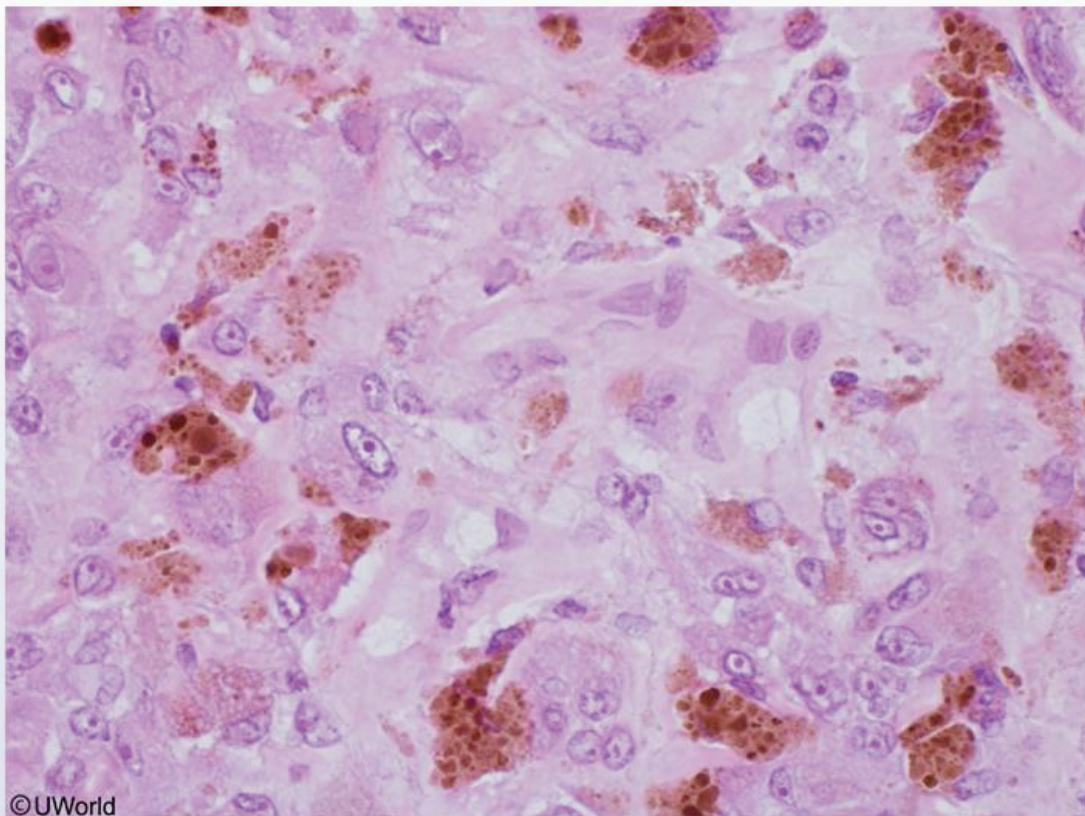
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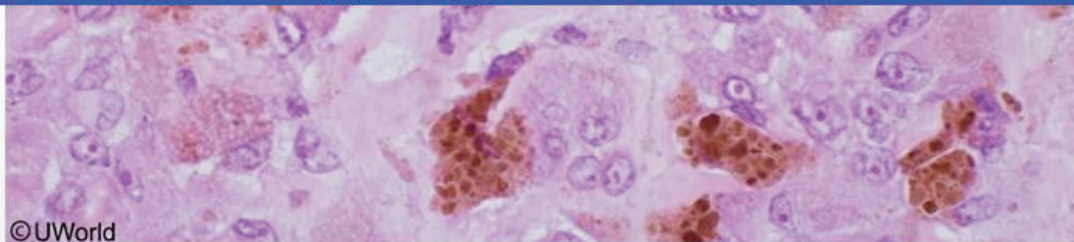
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Text Zoom



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These histopathologic findings are most consistent with which of the following diagnoses?

- ☐ A. Chronic systolic heart failure
- ☐ B. Emphysema
- ☐ C. Hodgkin lymphoma
- ☐ D. Metastatic melanoma
- ☐ E. Sarcoidosis
- ☐ F. Squamous cell lung cancer

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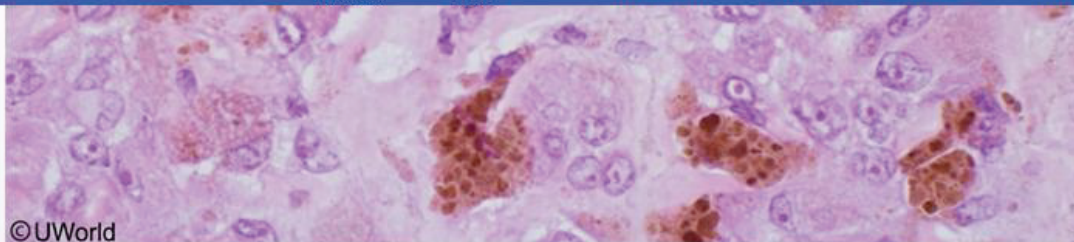
Notes

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Settings



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These histopathologic findings are most consistent with which of the following diagnoses?

- ☐ A. Chronic systolic heart failure (27%)
- ☐ B. Emphysema (1%)
- ☐ C. Hodgkin lymphoma (6%)
- ☒ D. Metastatic melanoma (57%)
- ☐ E. Sarcoidosis (4%)
- ☐ F. Squamous cell lung cancer (3%)

Correct

57%

18 secs

12/11/2020

Block Time Remaining: 00:23:22

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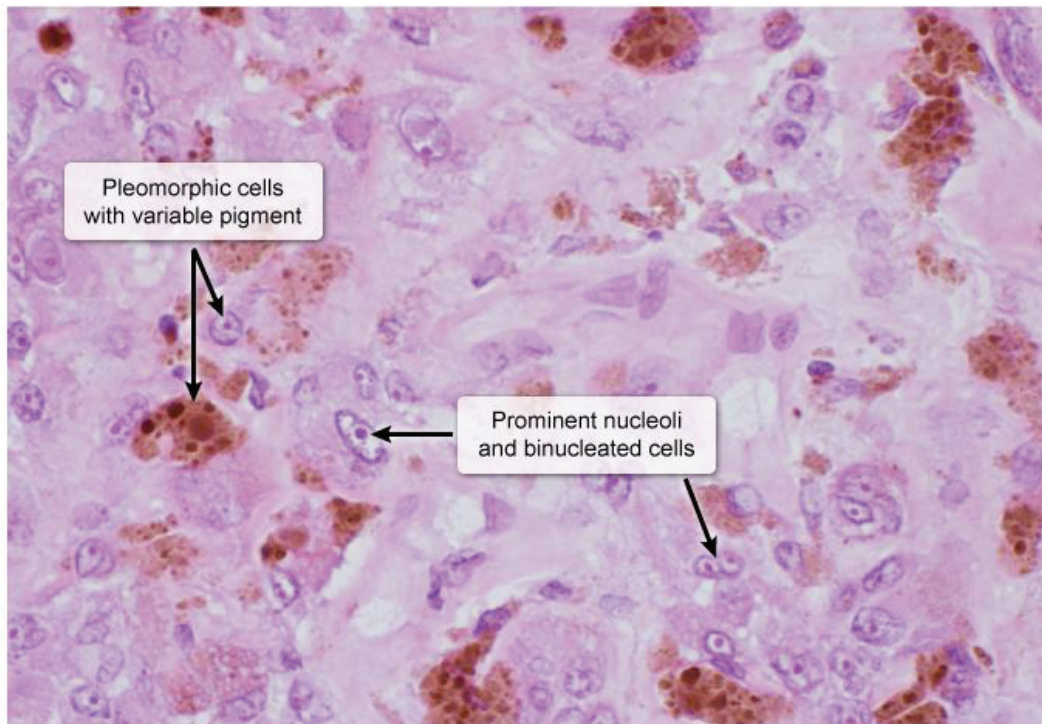


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### Metastatic melanoma



Histopathology from this patient's lung lesion reveals features concerning for **malignancy**, including disordered, pleomorphic cells; large nuclei; irregular nuclear shape and binucleation; as well as prominent nucleoli. Although he is at risk for primary lung cancer due to a long smoking history, the presence of **brown pigment** (melanin granules) in the cytoplasm of some of the atypical cells indicates likely **melanoma recurrence**.

Surgical resection of cutaneous melanoma is sometimes curative, but the tumor often spreads through the lymphatics and bloodstream to other organs early in the disease course; these metastases can remain asymptomatic for months to years. Recurrence is generally diagnosed when a suspicious lesion is identified and biopsy reveals malignant melanocytes (eg, cytoplasmic melanin, cellular atypia) with positive immunostaining for melanocytic markers (eg, **S-100**, **HMB-45**).

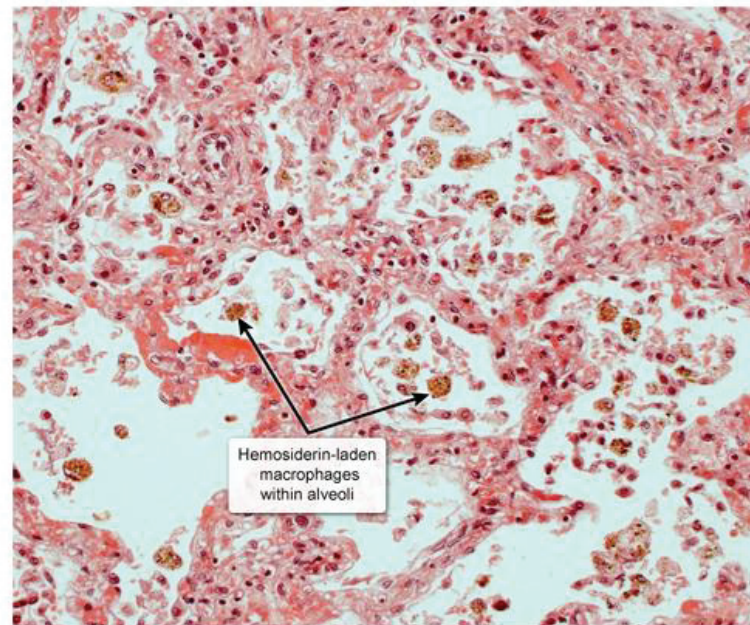
**(Choice A)** Chronic systolic heart failure can sometimes be associated with cough and fatigue due to **pulmonary congestion**. Although brown, hemosiderin-laden macrophages can be seen, atypical cells (eg, binucleated, enlarged nuclei) and hilar lymphadenopathy would not be present.

**(Choice B)** This patient is at risk for emphysema due to his long smoking history. Although **emphysema** often causes dyspnea and cough, biopsy would show airspace enlargement and destruction of alveolar walls.



Exhibit Display

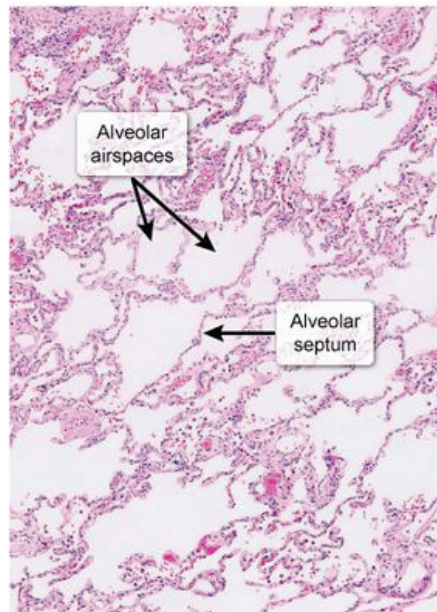
Chronic pulmonary congestion



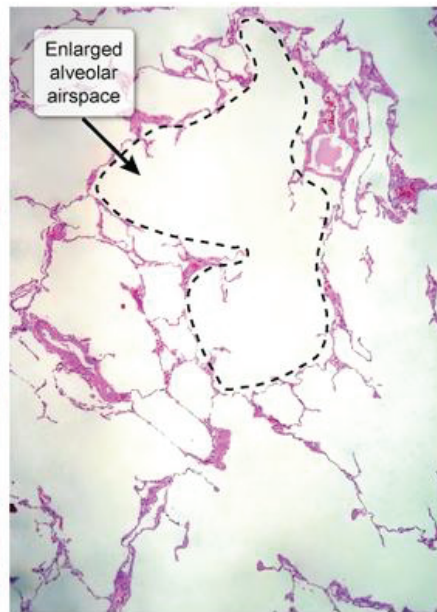
Hemosiderin-laden  
macrophages  
within alveoli

Exhibit Display

Normal lung



Emphysema



Zoom In

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**(Choice B)** This patient is at risk for emphysema due to his long smoking history. Although **emphysema** often causes dyspnea and cough, biopsy would show airspace enlargement and destruction of alveolar walls.

**(Choice C)** **Hodgkin lymphoma** frequently presents with diffuse lymphadenopathy or pulmonary symptoms (eg, cough) related to a mediastinal mass. However, biopsy would show malignant Reed-Sternberg cells amidst an inflammatory infiltrate (not cells with dark pigment).

**(Choice E)** **Sarcoidosis** frequently causes pulmonary symptoms and fatigue and often presents with hilar lymphadenopathy and reticular pulmonary infiltrates. However, biopsy would show noncaseating granulomas, not pigmented, atypical cells.

**(Choice F)** **Squamous cell lung cancer** frequently presents with cough and fatigue. Although atypical cells would be seen on biopsy, keratin (not brown pigment) would be present.

**Educational objective:**

Melanoma is a highly aggressive malignancy that often metastasizes early in the disease course. Patients may be asymptomatic for years prior to onset of metastatic manifestations. Diagnosis is generally made when a histopathologic sample shows cellular atypia with cells containing brown pigment (melanin granules); immunostaining for melanocytic markers (eg, S-100, HMB-45) is generally positive.







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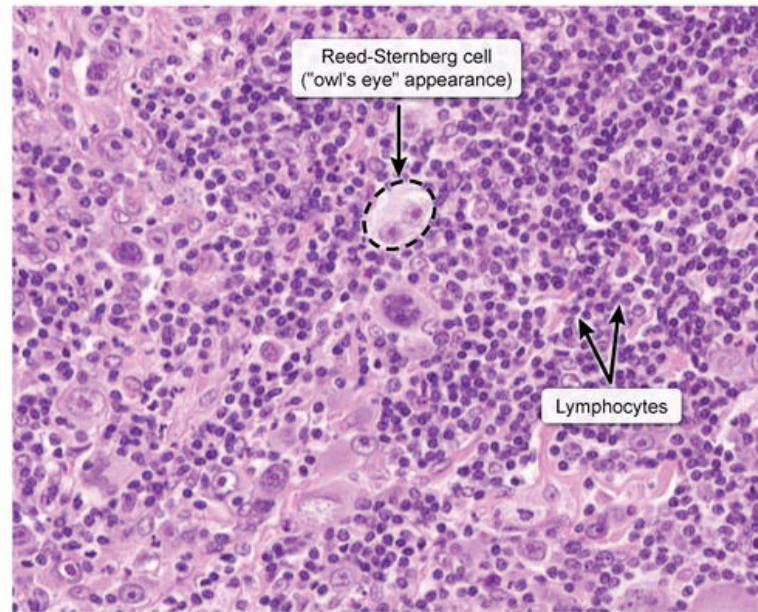
Text Zoom

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(Choice B) This patient is at risk for emphysema due to his long smoking history. Although emphysema

## Exhibit Display

## Hodgkin lymphoma



Reed-Sternberg cell  
("owl's eye" appearance)

Lymphocytes

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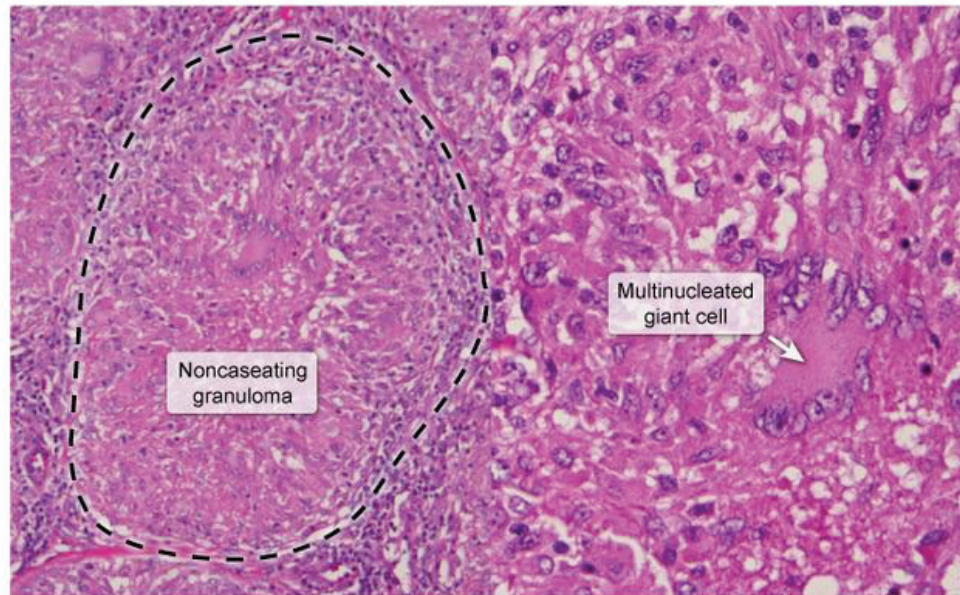
Text Zoom

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(Choice B) This patient is at risk for emphysema due to his long smoking history. Although emphysema

## Exhibit Display

## Sarcoidosis



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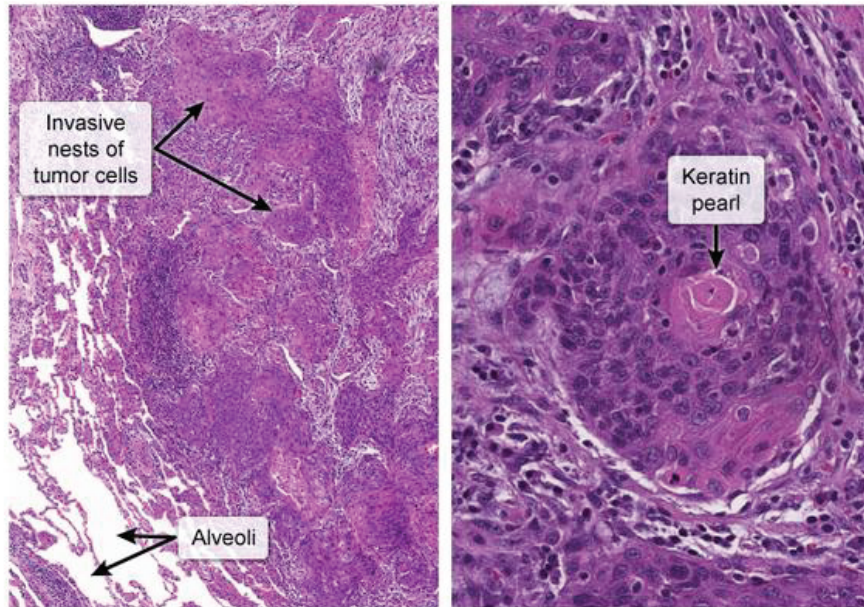
Text Zoom

Settings

(Choice B) This patient is at risk for emphysema due to his long smoking history. Although emphysema

## Exhibit Display

## Squamous cell carcinoma of the lung



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End Block





An 8-year-old girl is brought to the office for evaluation of a skin rash on her upper back. The rash is not painful but is mildly pruritic. She has no prior medical conditions, takes no medications, and is up to date with vaccinations. Vital signs are within normal limits. Right scapular area skin examination is shown in the [exhibit](#). The remainder of the examination is normal. Which of the following is the most likely cause of this patient's current condition?

- ☐ A. Deep tissue invasion by normal skin flora
- ☐ B. Epidermal damage from excessive sun exposure
- ☐ C. Immunologic response to bacterial pharyngitis
- ☐ D. Microbial infection of keratinized structures
- ☐ E. Proliferation of pathogen transmitted by tick bite

**Submit**

Exhibit Display



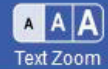
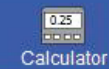
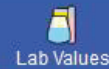
Zoom In

Zoom Out

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An 8-year-old girl is brought to the office for evaluation of a skin rash on her upper back. The rash is not painful but is mildly pruritic. She has no prior medical conditions, takes no medications, and is up to date with vaccinations. Vital signs are within normal limits. Right scapular area skin examination is shown in the [exhibit](#). The remainder of the examination is normal. Which of the following is the most likely cause of this patient's current condition?

- ☐ A. Deep tissue invasion by normal skin flora (6%)
- ☐ B. Epidermal damage from excessive sun exposure (3%)
- ☐ C. Immunologic response to bacterial pharyngitis (19%)
- ☒ D. Microbial infection of keratinized structures (65%)
- ☐ E. Proliferation of pathogen transmitted by tick bite (4%)

Correct

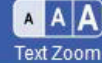
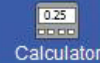
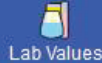
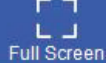
65%  
Answered correctly

01 min, 56 secs  
Time Spent

02/27/2021  
Last Updated







This patient, with a mildly pruritic, polycyclic rash with a raised, scaly border and central clearing, has **tinea corporis**. Patches of tinea corporis are typically round or ovoid but may become confluent to form a "flower petal" shape. Skin contact, especially in warm and humid environments, is a common risk factor, and patients often have concurrent infections in other body areas. Any species of dermatophyte may cause this condition, but *Trichophyton rubrum* is the most frequent culprit.

**Dermatophyte infections** (eg, tinea corporis, tinea pedis, tinea cruris) infect keratinized matter in the **stratum corneum** of the **superficial epidermis** but do not invade the dermis and subcutaneous tissues. The diagnosis is confirmed with potassium hydroxide (KOH) preparation of skin scrapings, which can show the characteristic segmented hyphae and arthrospores.

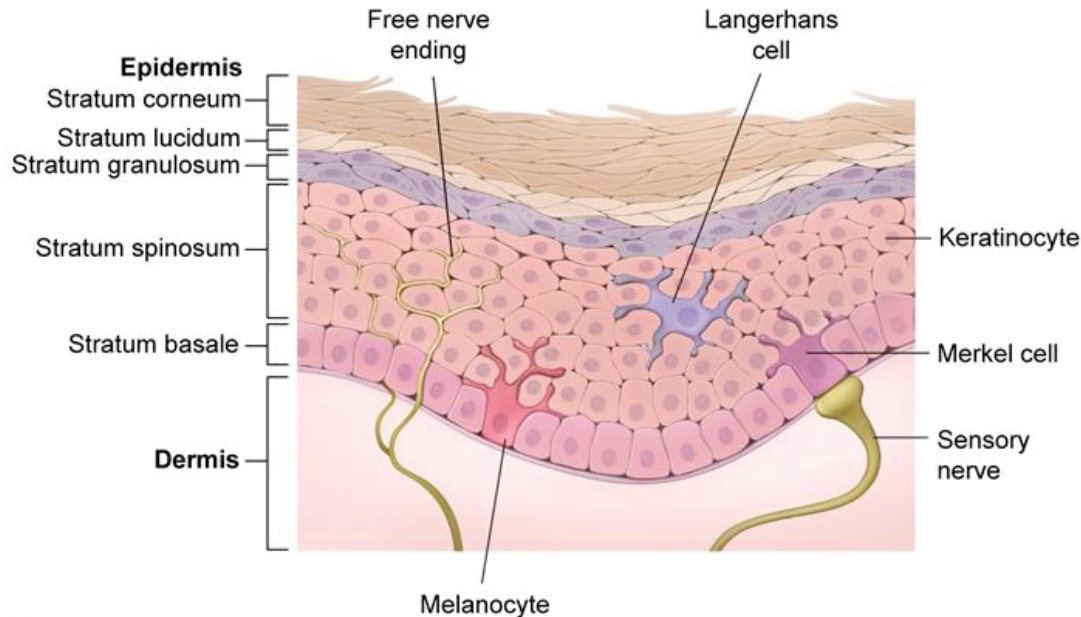
**(Choice A)** Cutaneous candidiasis (eg, **intertrigo**) is an inflammatory condition involving approximated skin surfaces such as the axillae, groin, inframammary folds, or abdominal folds. *Candida albicans* is a commensal organism that is normally present on the skin and can become invasive if there is disruption in the normal skin barrier.

**(Choice B)** Sunburn presents with erythema, itching, and pain in sun-exposed areas. Sunburned skin may undergo superficial desquamation (peeling), but this patient's rounded lesions with peripheral scaling



Exhibit Display

Layers of the epidermis



Zoom In

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Exhibit Display



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**(Choice B)** Sunburn presents with erythema, itching, and pain in sun-exposed areas. Sunburned skin may undergo superficial desquamation (peeling), but this patient's rounded lesions with peripheral scaling are more consistent with tinea corporis.

**(Choice C)** Patients with untreated streptococcal pharyngitis can develop **erythema marginatum**, a fleeting pink or red rash with central clearing that can appear, disappear, and reappear within hours. This is a hallmark feature of rheumatic fever and is usually accompanied by other signs such as migratory arthritis, carditis, subcutaneous nodules, and Sydenham chorea.

**(Choice E)** Acute Lyme disease is characterized by flu-like symptoms and **erythema migrans**, a slowly spreading erythematous rash with central clearing at the site of the tick bite. Disseminated disease can present with multiple lesions, but the lesions are flat or only slightly raised and the border is indistinct rather than scaly; they often develop a targetoid appearance.

### Educational objective:

Tinea corporis presents with round or ovoid lesions with a raised, scaly border and central clearing.

*Trichophyton rubrum* is the most common cause and infects keratinized matter in the stratum corneum of the superficial epidermis but does not invade the dermis and subcutaneous tissues.

### References



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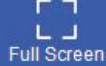
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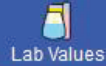
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Full Screen



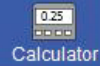
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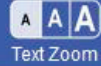
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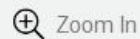


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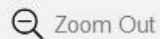


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## Exhibit Display



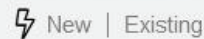
Zoom In



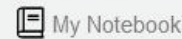
Zoom Out



Reset



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Suspend



End Block



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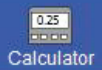
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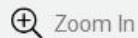


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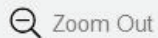


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## Exhibit Display



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A 38-year-old woman comes to the office for evaluation of a skin lesion. It began as a pink papule on her right arm and has progressively enlarged over several weeks. The lesion is not pruritic or painful and has not been associated with fever or other systemic symptoms. The patient returned from a trip to Costa Rica 5 weeks ago. During her travel, she stayed at a beachside resort and hiked in the rainforest. Skin examination findings are shown below. Biopsy of the lesion reveals intracellular, round-oval protozoa with rod-shaped kinetoplasts. Which of the following most likely led to this patient's current condition?



Exhibit Display



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- ☐ A. Bite from infected sand fly
- ☐ B. Contact with infected person
- ☐ C. Exposure to decaying vegetation
- ☐ D. Handling of infected animal
- ☐ E. Swimming in contaminated water

**Submit**

1



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Suspend



End Block





- ✓ ☒ A. Bite from infected sand fly (52%)
- ☐ B. Contact with infected person (4%)
- ☐ C. Exposure to decaying vegetation (7%)
- ☐ D. Handling of infected animal (7%)
- ☐ E. Swimming in contaminated water (29%)

Correct

52%



01 min, 37 secs



02/13/2021

Block Time Remaining: 00:26:56

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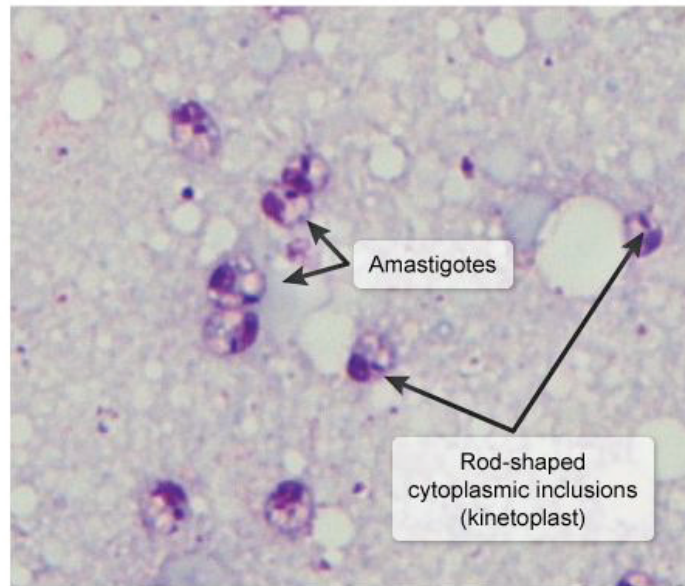


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## Leishmaniasis



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Microscopy of this patient's skin lesion revealed intracellular protozoa with rod-shaped kinetoplasts, raising strong suspicion for **cutaneous leishmaniasis**, a parasitic disease endemic to the Middle East and Central



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Microscopy of this patient's skin lesion revealed intracellular protozoa with rod-shaped kinetoplasts, raising strong suspicion for **cutaneous leishmaniasis**, a parasitic disease endemic to the Middle East and Central and South America. *Leishmania* species are harbored by small mammals and transmitted to humans via bites from **infected sand flies**. The parasite subsequently matures within mammalian macrophages and can be visualized on biopsy as **intracellular, round-oval** amastigotes with **rod-shaped kinetoplasts** (see arrow).

Cutaneous leishmaniasis is characterized by a chronic, **enlarging, pinkish papule** at the site of the bite that eventually develops into a nodule or **plaque** and ulcerates. Most cases occur on exposed areas of skin because sand fly bites cannot penetrate clothing. More serious mucosal or lymphatic *Leishmania* infections can also occur.

**(Choice B)** Yaws, a spirochetal infection caused by *Treponema pallidum* subspecies, is transmitted by skin-to-skin (nonsexual) contact and is seen in Central America. Patients typically develop a painless papule that eventually ulcerates (similar to syphilitic chancre). However, this organism is a bacterium, not a protozoan.

**(Choice C)** *Sporothrix schenckii*, a dimorphic fungus, grows in decaying plant matter and is transmitted to humans via subcutaneous inoculation. Manifestations include a papule at the site of inoculation and







protozoan.

**(Choice C)** *Sporothrix schenckii*, a dimorphic fungus, grows in decaying plant matter and is transmitted to humans via subcutaneous inoculation. Manifestations include a papule at the site of inoculation and subsequent papules along proximal lymphatic drainage pathways. Histopathology demonstrates granulomas and cigar-shaped, budding fungus.

**(Choice D)** *Bacillus anthracis*, a gram-positive bacterial infection, is often transmitted to humans due to cutaneous contact with infected animals or animal hides. Manifestations include a painless cutaneous papule that evolves over days into an ulcer with a black eschar. Histopathology would show extracellular, gram-positive rods.

**(Choice E)** *Mycobacterium marinum*, an acid-fast bacterium, causes cutaneous infection after exposure to contaminated water (eg, fish tank). Patients typically develop a papule that ulcerates and scars. However, histopathology would not show intracellular protozoa.

### Educational objective:

*Leishmania* species are obligate intracellular protozoa that mature in macrophages and can be identified on biopsy by the presence of rod-shaped kinetoplasts. They are transmitted to humans by infected sand flies and cause the clinical syndrome of cutaneous leishmaniasis, characterized by a chronic, pinkish papule



humans via subcutaneous inoculation. Manifestations include a papule at the site of inoculation and subsequent papules along proximal lymphatic drainage pathways. Histopathology demonstrates granulomas and cigar-shaped, budding fungus.

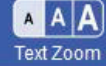
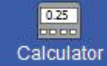
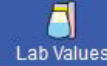
**(Choice D)** *Bacillus anthracis*, a gram-positive bacterial infection, is often transmitted to humans due to cutaneous contact with infected animals or animal hides. Manifestations include a painless cutaneous papule that evolves over days into an ulcer with a black eschar. Histopathology would show extracellular, gram-positive rods.

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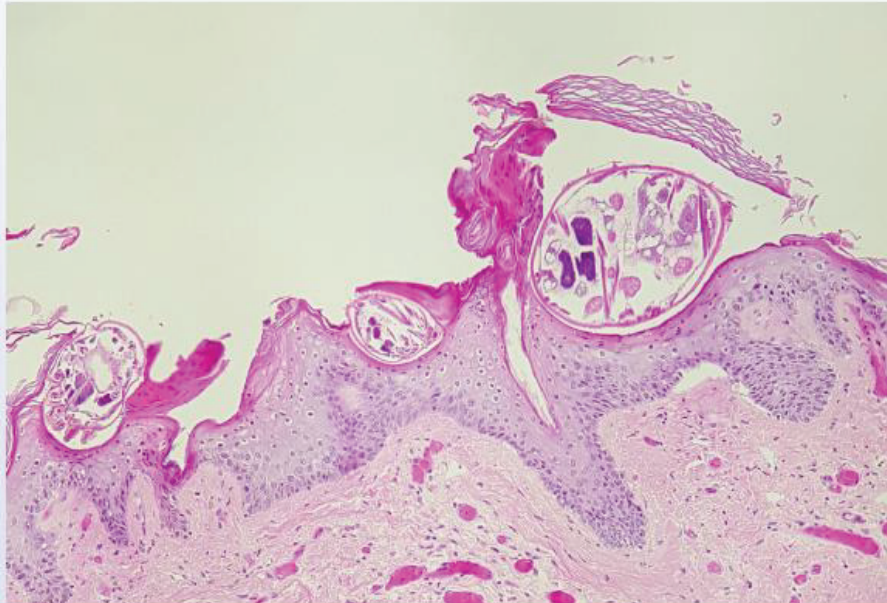
**Educational objective:**

*Leishmania* species are obligate intracellular protozoa that mature in macrophages and can be identified on biopsy by the presence of rod-shaped kinetoplasts. They are transmitted to humans by infected sand flies and cause the clinical syndrome of cutaneous leishmaniasis, characterized by a chronic, pinkish papule that evolves into a nodule or plaque.





A 29-year-old man is evaluated for a skin rash involving his hands, feet, and scalp for the last 2 weeks. The rash is mildly pruritic and has progressively worsened. The patient has a history of HIV and is not adherent with antiretroviral therapy. Skin examination shows erythematous patches with scales and crusting. Biopsy of the rash shows organisms burrowed in the epidermis, as shown below:







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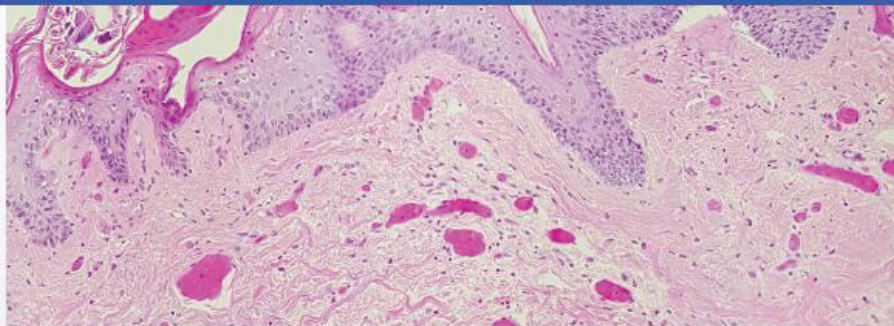
Notes

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Text Zoom

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Which of the following is the most appropriate treatment for this patient?

- ☐ A. Systemic acyclovir
- ☐ B. Systemic terbinafine
- ☐ C. Topical glucocorticoid
- ☐ D. Topical mupirocin
- ☐ E. Topical permethrin

**Submit**

Block Time Remaining: 00:27:04

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Tutorial

Lab Values

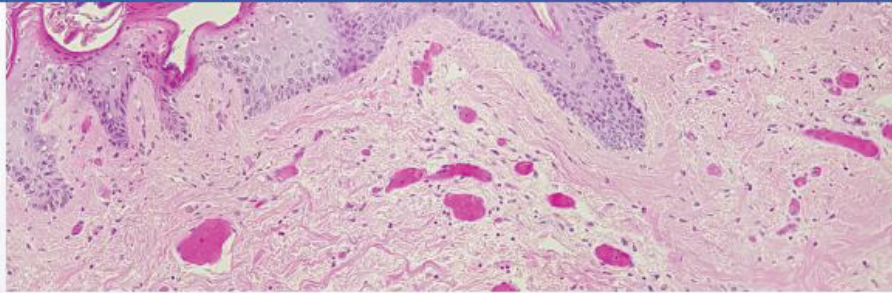
Notes

Calculator

Reverse Color

Text Zoom

Settings



Which of the following is the most appropriate treatment for this patient?

- ☐ A. Systemic acyclovir (5%)
- ☐ B. Systemic terbinafine (20%)
- ☐ C. Topical glucocorticoid (3%)
- ☐ D. Topical mupirocin (6%)
- ☒ E. Topical permethrin (63%)

Correct

63%

19 secs

11/12/2020

Block Time Remaining: 00:27:15

TUTOR

<https://t.me/USMLEWorldStep1>

## Scabies







Mark



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Settings

**Scabies** is a skin infection caused by the **human itch mite**, *Sarcoptes scabiei*. Transmission occurs from prolonged skin-to-skin contact with an infected individual but may occasionally occur due to contact with contaminated fomites (eg, bedsheets, clothing). Mites **burrow under the epidermis** and evoke a delayed-type hypersensitivity reaction to mite feces and eggs, which leads to an intensely **pruritic rash**. The mites can often be seen on microscopy.

Classic scabies is associated with a mild mite burden (10-15 mites). Patients usually have several small erythematous papules on the sides/webs of the fingers, wrists, elbows, axillae, waist, and genitalia.

**Excoriations** and **burrows** (thin, serpiginous red tracks) may be seen. In contrast, patients with impaired cell-mediated immunity (eg, **HIV**) are unable to contain the infection and usually develop **crusted scabies**, which is associated with thousands or **millions of mites**. These patients often have mild pruritis (because the inflammatory response is muted) and several erythematous patches with scaling and crusting.

Treatment is required to prevent discomfort, transmission, and potential complications (eg, secondary bacterial infection). First-line therapy includes **topical permethrin**, which blocks mite neurotransmission by impairing voltage-gated sodium channels. Oral **ivermectin**, an antiparasitic agent that binds chloride ion channels in invertebrate nerve and muscle cells, is an alternate medication for classic scabies that is used in combination with permethrin for crusted scabies.



0



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Suspend



End Block



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## Exhibit Display



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Settings

used in combination with permethrin for crusted scabies.

**(Choice A)** Oral acyclovir is used for human **herpes simplex virus** outbreaks, which are usually characterized by vesicular lesions on an erythematous base. The orolabial mucosa and genital area are affected most commonly. Histopathology would show epidermal blisters with acantholysis and multinucleated cells.

**(Choice B)** Oral terbinafine can be used for patients with dermatophytic infections of the skin. Dermatophytes often cause an erythematous scaly rash and erosions. Microscopy typically reveals fungal spores and/or hyphae.

**(Choice C)** **Psoriasis** is a chronic inflammatory skin condition that can be treated with topical glucocorticoids. It is usually associated with symmetric, **sharply defined skin plaques** with overlying scales on the extensor elbows, knees, and scalp. Microscopy generally shows uniform epidermal hyperplasia, parakeratosis, dilated capillaries in the papillary dermis, and perivascular lymphocytes.

**(Choice D)** Topical mupirocin is used for the treatment of impetigo, a superficial bacterial infection caused by *Staphylococcus aureus* and *Streptococcus pyogenes*. The condition typically presents as a localized papulovesicular rash with surrounding erythema and adherent golden crusts involving the face or extremities.

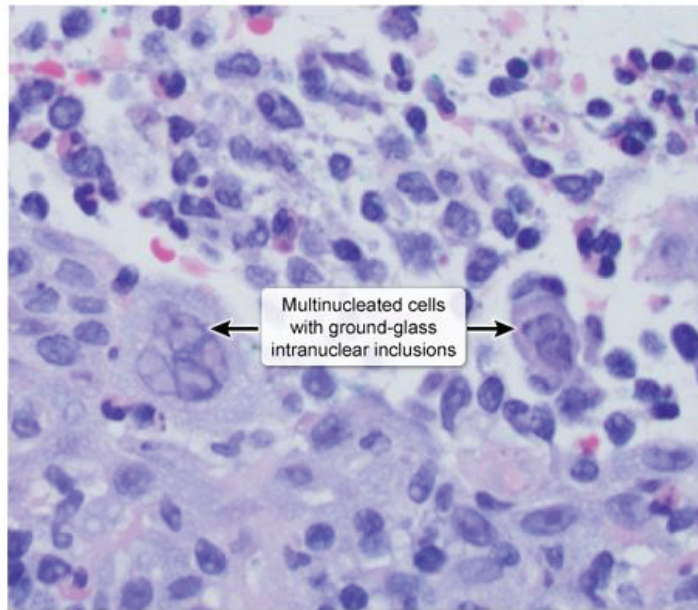




used in combination with permethrin for crusted scabies.

## Exhibit Display

## Vulvar herpes simplex (HSV)



Multinucleated cells  
with ground-glass  
intranuclear inclusions

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Zoom Out

Reset

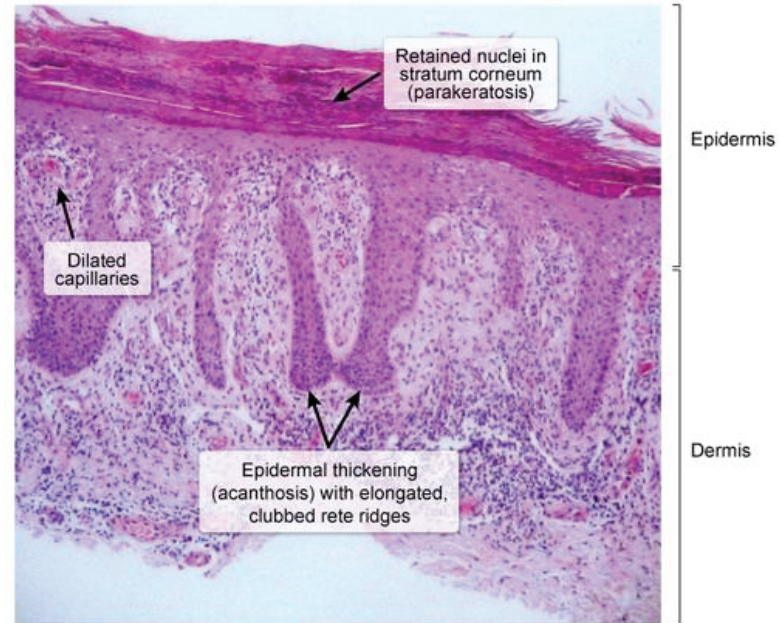
New | Existing

My Notebook

used in combination with permethrin for crusted scabies.

## Exhibit Display

## Psoriasis



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used in combination with permethrin for crusted scabies.

## Exhibit Display



Zoom In

Zoom Out

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My Notebook





**(Choice C)** Psoriasis is a chronic inflammatory skin condition that can be treated with topical glucocorticoids. It is usually associated with symmetric, sharply defined skin plaques with overlying scales on the extensor elbows, knees, and scalp. Microscopy generally shows uniform epidermal hyperplasia, parakeratosis, dilated capillaries in the papillary dermis, and perivascular lymphocytes.

**(Choice D)** Topical mupirocin is used for the treatment of impetigo, a superficial bacterial infection caused by *Staphylococcus aureus* and *Streptococcus pyogenes*. The condition typically presents as a localized papulovesicular rash with surrounding erythema and adherent golden crusts involving the face or extremities.

### Educational objective:

Scabies is a human mite infection associated with a pruritic papular rash with excoriations and burrows. Patients with impaired cell-mediated immunity (eg, HIV) often develop a very high mite burden. Treatment with topical permethrin and/or ivermectin is generally curative.

Microbiology

Dermatology

Scabies

Subject

System

Topic

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A 28-year-old man comes to the office to discuss hair loss. He has hair loss primarily around the temples, which began insidiously 3 years ago. The patient is concerned because several of his family members became almost completely bald by their late 30s. He otherwise feels healthy and has normal muscle strength, libido, and erectile function. The patient is married, has 2 children, and works as a charter airplane pilot. Physical examination shows moderate thinning of hair at the anterior scalp, temporal region, and vertex. An oral medication is prescribed to treat the hair loss. After the initiation of therapy, which of the following changes would most likely occur in this patient?

**Testosterone   Dihydrotestosterone   Estradiol**

- ☐ A. Decreased   Decreased   Decreased
- ☐ B. Decreased   Decreased   Increased
- ☐ C. Decreased   Increased   Increased
- ☐ D. Increased   Decreased   Increased
- ☐ E. Increased   Increased   Decreased



which began insidiously 3 years ago. The patient is concerned because several of his family members became almost completely bald by their late 30s. He otherwise feels healthy and has normal muscle strength, libido, and erectile function. The patient is married, has 2 children, and works as a charter airplane pilot. Physical examination shows moderate thinning of hair at the anterior scalp, temporal region, and vertex. An oral medication is prescribed to treat the hair loss. After the initiation of therapy, which of the following changes would most likely occur in this patient?

**Testosterone   Dihydrotestosterone   Estradiol**

- ☐ A. Decreased   Decreased   Decreased (3%)
- ☐ B. Decreased   Decreased   Increased (10%)
- ☐ C. Decreased   Increased   Increased (5%)
- ☒ D. Increased   Decreased   Increased (67%)
- ☐ E. Increased   Increased   Decreased (13%)

Correct

67%

01 min, 11 secs

09/24/2020

Block Time Remaining: 00:28:26

TUTOR

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block



Androgenetic (male pattern) alopecia in men	
Pathophysiology	<ul style="list-style-type: none"><li>• Genetic factors + androgen (dihydrotestosterone) effect</li><li>• Shortened anagen phase</li><li>• Follicular miniaturization</li></ul>
Clinical features	<ul style="list-style-type: none"><li>• Onset at puberty, progressive course</li><li>• Hair loss at temporal, frontal, vertex scalp</li><li>• Shorter, thinner, sparser hair</li></ul>
Treatment	<ul style="list-style-type: none"><li>• Minoxidil</li><li>• 5-alpha reductase inhibitors (eg, finasteride)</li></ul>

This patient has **androgenetic alopecia** (often called male pattern hair loss), which presents with **progressive hair loss** at the temples, frontal hairline, and vertex. Androgenetic alopecia is characterized by a shortened anagen hair growth phase in the affected portions of the scalp, leading to shorter, thinner hair shafts (**follicular miniaturization**) with increased apoptosis at the dermal papillae.

As the name implies, androgenetic alopecia is driven by both inherited (polygenic inheritance) and

### Exhibit Display

#### Androgenetic alopecia

Stage 1



Stage 2



Stage 3



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Zoom In

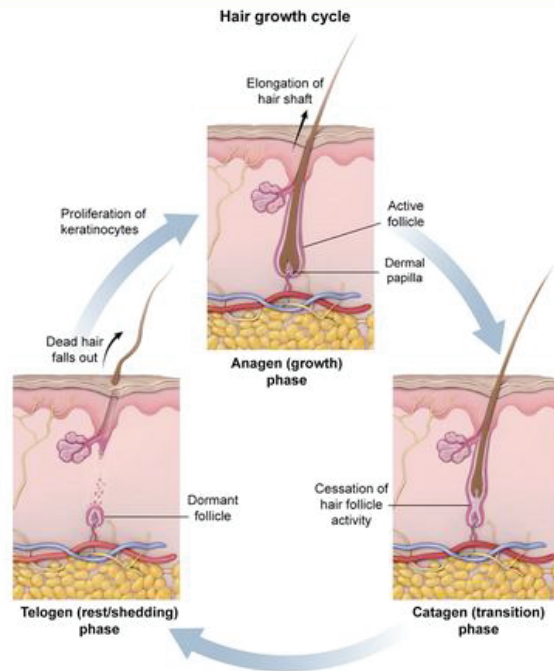
Zoom Out

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### Exhibit Display



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Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

hair shafts (**follicular miniaturization**) with increased apoptosis at the dermal papillae.

As the name implies, androgenetic alopecia is driven by both inherited (polygenic inheritance) and hormonal factors. **Dihydrotestosterone** (DHT) appears to be the primary androgen responsible for hair loss. Although total androgen levels are similar in affected and unaffected men, patients with androgenetic alopecia have a greater effect of DHT due to increased local conversion of testosterone to DHT and increased concentrations of androgen receptors in affected areas of the scalp.

Androgenetic alopecia can be treated with **5-alpha reductase inhibitors** (eg, **finasteride**), which **decrease** conversion of testosterone to **DHT** in the tissues. However, by preventing conversion to DHT, they **increase the level of testosterone**, which is then available for conversion to **estradiol** by aromatase.

This can lead to mild feminizing effects (eg, gynecomastia) in some patients. Other treatments for androgenetic alopecia include topical minoxidil, a vasodilator that appears to increase the vascularity of the dermal papillae.

**(Choices A, B, C, and E)** Inhibition of 5-alpha reductase by finasteride lowers DHT formation, leading to higher levels of testosterone and increased conversion to estradiol.

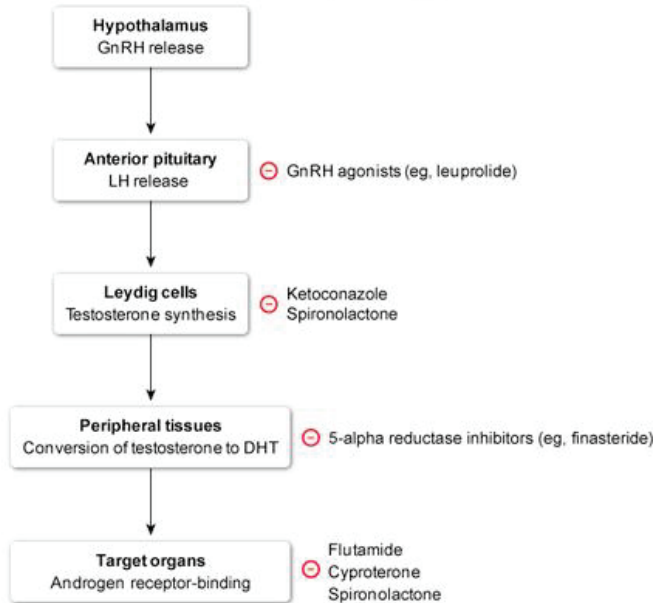
### Educational objective:

Androgenetic alopecia causes hair loss primarily at the anterior scalp and vertex. It shows polygenic



### Exhibit Display

#### Antiandrogen therapy



DHT = dihydrotestosterone

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Androgenetic alopecia can be treated with **5-alpha reductase inhibitors** (eg, **finasteride**), which **decrease** conversion of testosterone to **DHT** in the tissues. However, by preventing conversion to DHT, they **increase the level of testosterone**, which is then available for conversion to **estradiol** by aromatase. This can lead to mild feminizing effects (eg, gynecomastia) in some patients. Other treatments for androgenetic alopecia include topical minoxidil, a vasodilator that appears to increase the vascularity of the dermal papillae.

**(Choices A, B, C, and E)** Inhibition of 5-alpha reductase by finasteride lowers DHT formation, leading to higher levels of testosterone and increased conversion to estradiol.

### Educational objective:

Androgenetic alopecia causes hair loss primarily at the anterior scalp and vertex. It shows polygenic inheritance, with dihydrotestosterone (DHT) being the primary pathogenic factor. Five-alpha reductase inhibitors decrease the conversion of testosterone to DHT and are effective for treating the condition.

### References

- [The efficacy and safety of 5a-reductase inhibitors in androgenetic alopecia: a network meta-analysis and benefit-risk assessment of finasteride and dutasteride.](#)



1



Feedback



Suspend



End Block

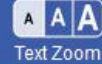
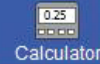
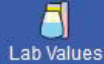
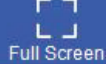




A 79-year-old woman comes to the office due to bleeding from an ulcerative lesion on her right nipple. The lesion is itchy, has been there for several months, and is slowly increasing in size. Examination shows a crusty, thickened, erythematous, and ulcerated nodule with evidence of hyperpigmentation. Changes extend to the surrounding areola. Excisional biopsy reveals relatively well-circumscribed aggregates of large, polygonal, pleomorphic cells with abundant mitotic activity and surrounding necrosis. S-100 and HMB-45 stains are diffusely positive. Which of the following is the most likely diagnosis?

- ☐ A. Basal cell carcinoma
- ☐ B. Melanoma
- ☐ C. Paget disease of the breast
- ☐ D. Seborrheic keratosis
- ☐ E. Squamous cell skin cancer

**Submit**



A 79-year-old woman comes to the office due to bleeding from an ulcerative lesion on her right nipple. The lesion is itchy, has been there for several months, and is slowly increasing in size. Examination shows a crusty, thickened, erythematous, and ulcerated nodule with evidence of hyperpigmentation. Changes extend to the surrounding areola. Excisional biopsy reveals relatively well-circumscribed aggregates of large, polygonal, pleomorphic cells with abundant mitotic activity and surrounding necrosis. S-100 and HMB-45 stains are diffusely positive. Which of the following is the most likely diagnosis?

- ☐ A. Basal cell carcinoma (2%)
- ☒ B. Melanoma (62%)
- ☐ C. Paget disease of the breast (30%)
- ☐ D. Seborrheic keratosis (0%)
- ☐ E. Squamous cell skin cancer (3%)

Correct

62%  
Answered correctly

49 secs  
Time Spent

02/21/2021  
Last Updated



This older patient has a crusted, ulcerated, hyperpigmented nodule on the nipple and areola. Biopsy was performed to differentiate Paget disease of the breast (**Choice C**), an adenocarcinoma of the areolar epithelium, from nodular **malignant melanoma**. Histopathology revealed poorly differentiated cells with abundant mitotic activity and necrosis. Subsequent immunostaining was positive for **S-100** (a protein expressed in cells derived from the **neural crest** such as melanocytes) and **HMB-45** (a monoclonal antibody that binds to **immature melanosomes** found in melanocytic tumors) indicating melanoma.

Immunostaining is often used to assist the diagnosis of melanoma because histopathologic features are sometimes insufficient to confirm the diagnosis. Tumor cells that stain **positive for multiple melanocyte markers** (as in this case) are very likely to be melanoma. S-100 is positive in >95% of melanoma tumors, and HMB-45 is both highly sensitive (>95%) and highly specific (~100%) for the malignancy.

**(Choice A)** Basal cell carcinoma usually appears on the face as a nodular, **flesh colored papule**. Although scaly trunk lesions can occasionally occur, this tumor is derived from basal epithelial cells and would not stain positive for melanocyte markers.

**(Choice D)** Seborrheic keratosis is a benign skin lesion that is well demarcated (appears "**stuck on**") with a verrucous surface. These lesions are derived from immature keratinocytes and would not stain positive for multiple melanin markers.



This older patient has a crusted, ulcerated, hyperpigmented nodule on the nipple and areola. Biopsy was

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This older patient has a crusted, ulcerated, hyperpigmented nodule on the nipple and areola. Biopsy was

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**(Choice A)** Basal cell carcinoma usually appears on the face as a nodular, flesh colored papule. Although scaly trunk lesions can occasionally occur, this tumor is derived from basal epithelial cells and would not stain positive for melanocyte markers.

**(Choice D)** Seborrheic keratosis is a benign skin lesion that is well demarcated (appears "stuck on") with a verrucous surface. These lesions are derived from immature keratinocytes and would not stain positive for multiple melanin markers.

**(Choice E)** Squamous cell carcinoma is most common on the head and neck but can also occasionally arise on the trunk. It generally appears as hyperkeratotic plaque, nodule, or papule. Because it is derived from epithelial cells (not melanocytes), multiple melanin markers would not be positive.

### Educational objective:

Melanoma is often diagnosed when immunostaining of biopsy samples reveals multiple melanocyte markers (eg, S-100, HMB-45, MART-1).

Pathology

Dermatology

Melanoma

Subject

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Topic

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(Choice A) Basal cell carcinoma usually appears on the face as a nodular flesh colored papule. Although

Exhibit Display



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Feedback



Suspend



End Block

A 52-year-old woman comes to the office with a 2-month history of oral lesions that cause pain with chewing and swallowing food. The patient did not seek treatment as she thought they would "go away on their own," but the lesions have persisted. On examination, there are erosions of the buccal and gingival mucosa as shown in the image below. There are several flaccid bullae with erosions scattered over her trunk. The blisters spread laterally with pressure, and traction on seemingly uninvolved skin produces blistering. Autoantibodies directed against which of the following structures are most likely responsible for this process?



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- ☐ A. Basement membrane
- ☐ B. Connexin proteins
- ☐ C. Desmosomes
- ☐ D. Hemidesmosomes
- ☐ E. Tissue transglutaminase

Submit



- ☐ A. Basement membrane (2%)
- ☐ B. Connexin proteins (1%)
- ✓ ☒ C. Desmosomes (75%)
- ☐ D. Hemidesmosomes (19%)
- ☐ E. Tissue transglutaminase (1%)

Correct

75%  
Answered correctly

59 secs  
Time Spent

12/25/2020  
Last Updated

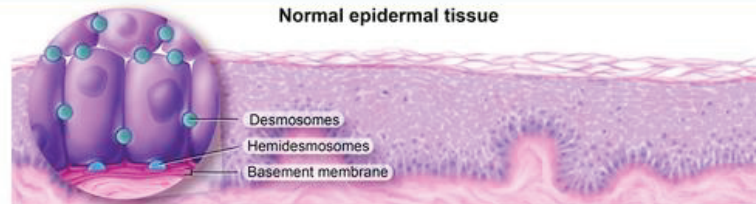
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<https://t.me/USMLEWorldStep1>



### Exhibit Display

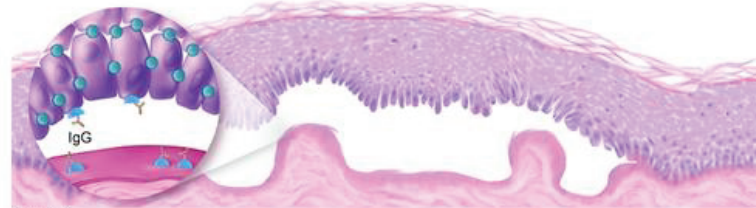
#### Normal epidermal tissue



#### Pemphigus vulgaris



#### Bullous pemphigoid



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## Exhibit Display



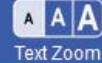
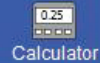
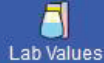
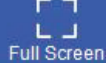
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This patient has **pemphigus vulgaris** (PV), an autoimmune bullous disease characterized by painful flaccid bullae and **erosions** of the skin and mucosal membranes. Any mucosal site can be involved, but the oral mucosa is the most common. The bullae are structurally weak and often rupture prior to presentation, with only erosions remaining. The bullae spread laterally when pressure is applied on top (Asboe-Hansen sign), and new blisters may form with gentle traction or rubbing (Nikolsky sign).

The underlying pathophysiology of PV involves autoantibodies directed against **desmosomes**, specifically **desmogleins** 1 and 3, which disrupt cohesion of keratinocytes. Biopsy of an active PV lesion will show **intraepithelial cleavage** with detached keratinocytes (acantholysis), retained keratinocytes along the basement membrane, and an eosinophilic inflammatory infiltrate. Direct immunofluorescence of unaffected skin adjacent to PV lesions will show epidermal intercellular IgG and C3 deposits. Circulating autoantibodies against desmoglein are present in many patients and can aid diagnosis.

**(Choice A)** Autoantibodies against cutaneous basement membrane proteins are characteristic of epidermolysis bullosa acquisita (forms tense acral bullae) and cicatricial pemphigoid (causes chronic conjunctivitis and scarring).

**(Choice B)** No known cutaneous diseases result from connexin autoimmunity, but connexin defects do underlie some specific forms of **palmoplantar keratoderma** or deafness-associated ichthiosis.





conjunctivitis and scarring).

**(Choice B)** No known cutaneous diseases result from connexin autoimmunity, but connexin defects do underlie some specific forms of **palmoplantar keratoderma** or deafness-associated ichthyosis.

**(Choice D)** Autoantibodies against hemidesmosomal proteins cause **bullous pemphigoid**, in which the bullae are usually tense and remain intact as the entire epidermis separates from the dermis (no intraepithelial cleavage). In addition, mucosal involvement is less common and Nikolsky sign is usually negative.

**(Choice E)** Autoantibodies against tissue transglutaminase result in **dermatitis herpetiformis** and celiac sprue.

### Educational objective:

Pemphigus vulgaris is an autoimmune bullous disease characterized by autoantibodies directed against desmosomal proteins (eg, desmoglein). It presents with painful flaccid bullae and erosions affecting the skin and mucosal membranes. The bullae spread laterally with pressure and new blisters may form with gentle rubbing.

### References

- **Correlation of conventional and conformational anti-desmoglein antibodies with phenotypes and**





conjunctivitis and scarring).

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

conjunctivitis and scarring).

Exhibit Display



Zoom In

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My Notebook

conjunctivitis and scarring).

Exhibit Display



Zoom In

Zoom Out

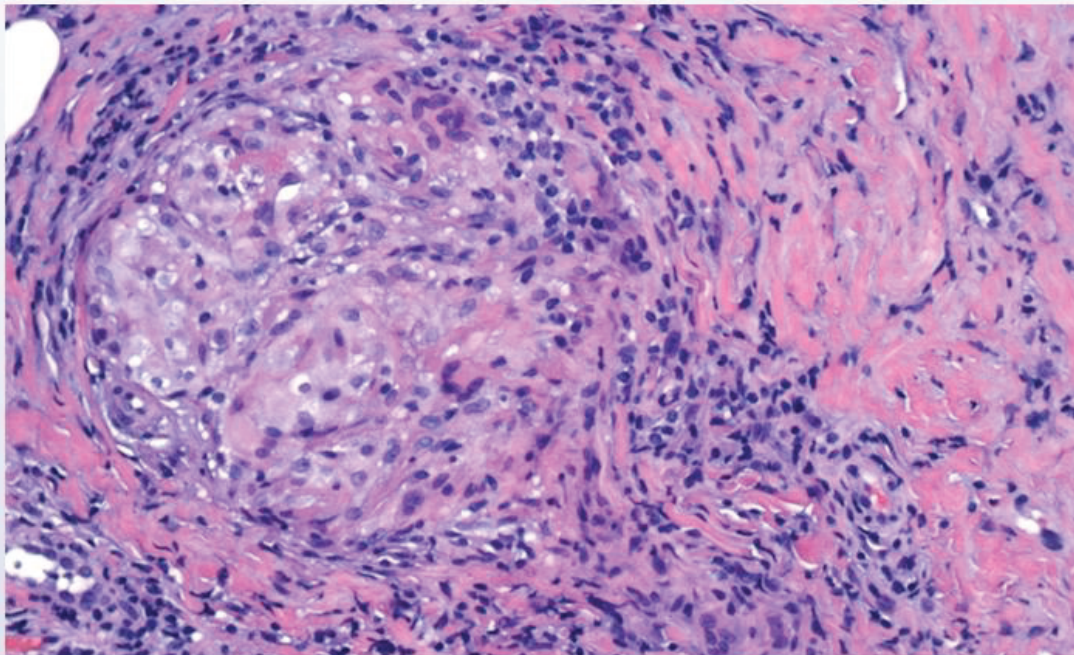
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A 19-year-old man comes to the office due to a painful subcutaneous forearm nodule. Two weeks earlier, he received a laceration on his left forearm while playing soccer and had sutures placed. The lesion is biopsied, and results are shown in the image below:





Mark



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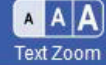
Notes



Calculator



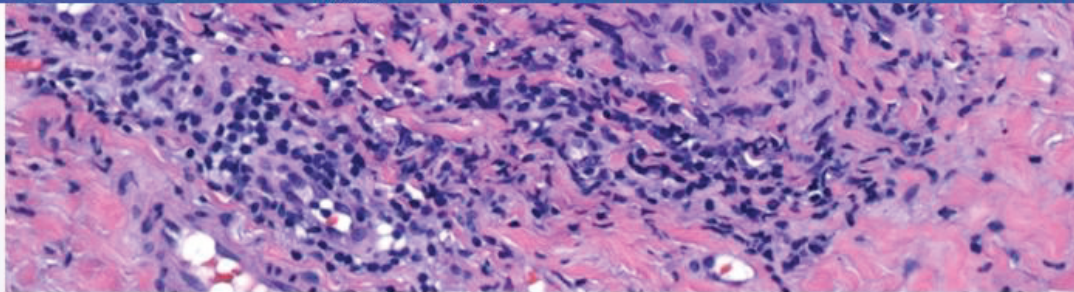
Reverse Color



Text Zoom



Settings



Which of the following is most likely responsible for this patient's condition?

- ☐ A. Excess granulation tissue formation
- ☐ B. Malignant transformation
- ☐ C. Normal wound remodeling
- ☐ D. Persistent neutrophil activity
- ☐ E. Reaction to a foreign body

**Submit**

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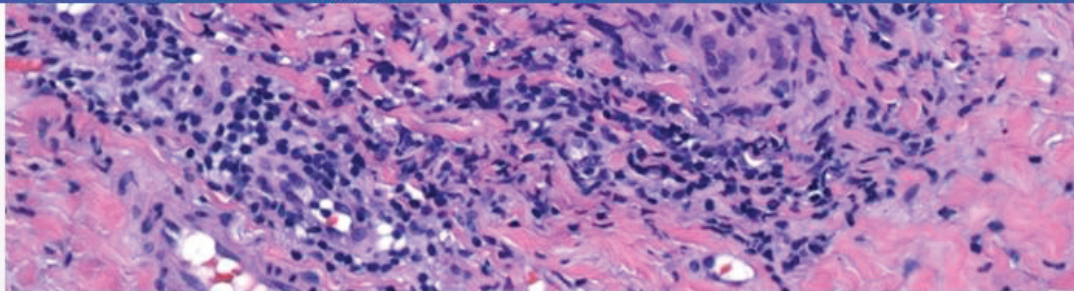
Feedback



Suspend



End Block



Which of the following is most likely responsible for this patient's condition?

- ☐ A. Excess granulation tissue formation (26%)
- ☐ B. Malignant transformation (0%)
- ☐ C. Normal wound remodeling (4%)
- ☐ D. Persistent neutrophil activity (13%)
- ☒ E. Reaction to a foreign body (54%)

Correct

54%



44 secs

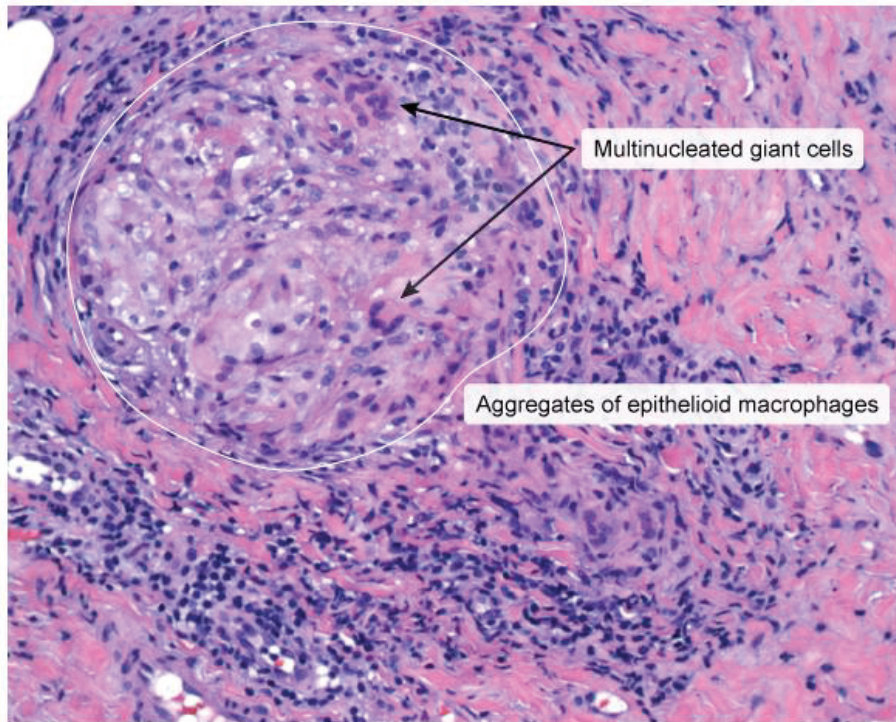


03/08/2021





## Granulomas



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**Foreign bodies** (eg, retained sutures) can elicit a granulomatous response, seen clinically as a tender, erythematous, brown or purple papule, nodule, or plaque. **Granulomas** are characterized microscopically by aggregates of **activated macrophages** that assume an epithelioid appearance. They are often surrounded by a rim of lymphocytes that synthesize the cytokines responsible for granuloma maintenance. Multinucleated giant cells, derived from the fusion of several macrophages, can also be found in granulomas.

Granuloma formation is a complex process that occurs over several **days to weeks** in response to an antigen that cannot be eradicated by more acute inflammatory mechanisms (eg, killing by neutrophils). As infiltrating macrophages engulf the antigenic debris, material resistant to digestion persists in the cytoplasm and causes macrophage activation. This results in further macrophage maturation and formation of a granuloma, which **walls off** the offending agent.

**(Choice A)** Excess **granulation tissue** formation (hypergranulation) usually occurs in a wound left to heal by secondary intention. Light microscopy would show proliferation of fibroblasts, collagen deposition, inflammatory cells, and numerous capillaries.

**(Choice B)** Marjolin ulcer is an aggressive, ulcerating squamous cell carcinoma that presents in an area of



0



Feedback

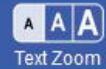
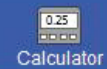
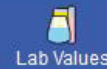


Suspend



End Block





**(Choice A)** Excess **granulation tissue** formation (hypergranulation) usually occurs in a wound left to heal by secondary intention. Light microscopy would show proliferation of fibroblasts, collagen deposition, inflammatory cells, and numerous capillaries.

**(Choice B)** Marjolin ulcer is an aggressive, ulcerating squamous cell carcinoma that presents in an area of previously traumatized, chronically inflamed, or scarred skin. Malignant transformation often occurs long after the initial trauma, usually >10 years later. Histology would show dysplastic keratinocytes and keratinization.

**(Choice C)** The remodeling phase of wound healing is characterized by fibrosis (scar formation) and starts the second week after injury. During this phase, active fibroblasts synthesize collagen, elastin, and other components of the connective tissue matrix.

**(Choice D)** The inflammatory phase of wound healing consists of the movement of neutrophils (within the first 24 hours) and macrophages (within 2-3 days) to the damaged area, with phagocytosis of necrotic debris and bacterial contaminants. Persistent neutrophil activity in a wound would result in an abscess and/or pus drainage rather than granuloma formation.

**Educational objective:**

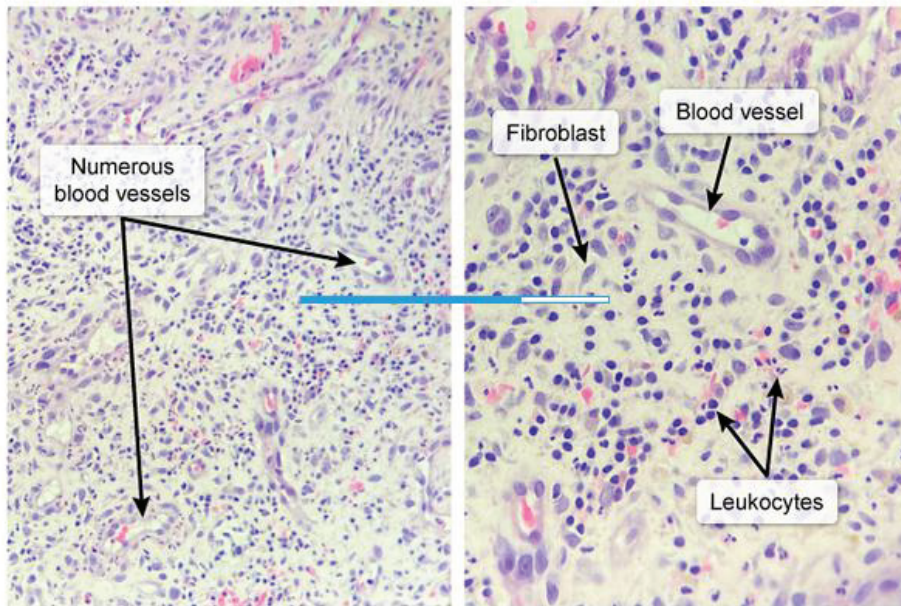
Granulomatous inflammation is a form of chronic inflammation characterized by aggregates of activated





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Granulation tissue



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after the initial trauma, usually >10 years later. Histology would show dysplastic keratinocytes and keratinization.

**(Choice C)** The remodeling phase of wound healing is characterized by fibrosis (scar formation) and starts the second week after injury. During this phase, active fibroblasts synthesize collagen, elastin, and other components of the connective tissue matrix.

**(Choice D)** The inflammatory phase of wound healing consists of the movement of neutrophils (within the first 24 hours) and macrophages (within 2-3 days) to the damaged area, with phagocytosis of necrotic debris and bacterial contaminants. Persistent neutrophil activity in a wound would result in an abscess and/or pus drainage rather than granuloma formation.

### Educational objective:

Granulomatous inflammation is a form of chronic inflammation characterized by aggregates of activated macrophages that assume an epithelioid appearance. Persistent granulomatous inflammation with subsequent fibrosis can cause organ dysfunction, which is seen in a number of granulomatous diseases.

Immunology

Dermatology

Skin and soft tissue infections

Subject

System

Topic

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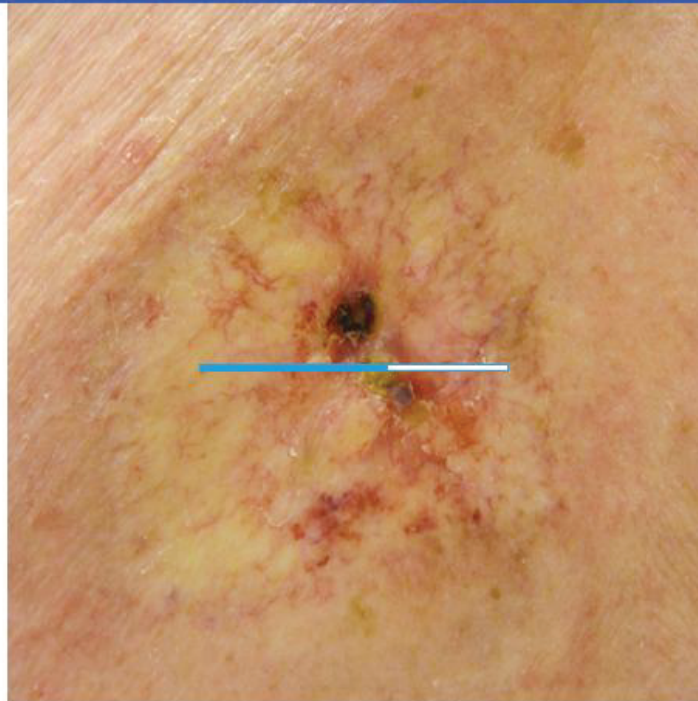
A 65-year-old man comes to the office due to 2 months of itching, occasional ulceration, and crusting of a skin lesion on his upper chest. A year ago, the patient was diagnosed with squamous cell carcinoma with perineural invasion at the site of the lesion. Surgical resection with clear margins was achieved, followed by adjuvant radiotherapy to the site. He reports no other symptoms. The patient's lesion is shown in the [exhibit](#). If a biopsy is performed at the periphery of the lesion, which of the following histologic changes is most likely to be seen?

- ☐ A. Full-thickness epidermal necrosis
- ☐ B. Homogenization of dermal collagen bundles
- ☐ C. Neutrophilic infiltrates and elongated dermal papillae
- ☐ D. Perivascular collections of eosinophils

**Submit**



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A 65-year-old man comes to the office due to 2 months of **itching**, occasional ulceration, and crusting of a skin lesion on his upper chest. A year ago, the patient was diagnosed with squamous cell carcinoma with perineural invasion at the site of the lesion. Surgical resection with clear margins was achieved, followed by adjuvant **radiotherapy** to the site. He reports no other symptoms. The patient's lesion is shown in the **exhibit**. If a biopsy is performed at the **periphery** of the lesion, which of the following histologic changes is most likely to be seen?

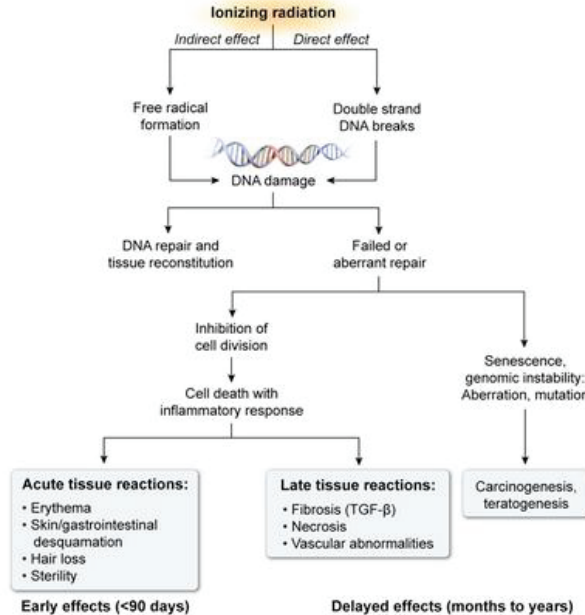
- ☐ A. Full-thickness epidermal necrosis (18%)
- ☒ B. Homogenization of dermal collagen bundles (47%)
- ☐ C. Neutrophilic infiltrates and elongated dermal papillae (23%)
- ☐ D. Perivascular collections of eosinophils (10%)

Correct

 47%  
Answered correctly 01 min, 45 secs  
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### Exhibit Display

#### Biologic effects of ionizing radiation



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This patient has a persistent, itchy, ulcerating skin lesion with **hypopigmentation** and **telangiectasias** at a site of prior radiotherapy, consistent with **late-stage radiation dermatitis**. Radiotherapy can be used with excision in the treatment of high-risk, invasive skin cancer to kill remaining cancer cells and decrease recurrence risk. **Ionizing radiation** causes **apoptosis** of rapidly dividing cancer cells directly by inducing **DNA damage** and indirectly by generating **free radicals**.

However, all **rapidly dividing cells** in the area (eg, hair follicle stem cells, melanocytes, basal keratinocytes) treated by the radiation can be affected, initiating a series of characteristic skin changes:

- Acute (<90 days after radiotherapy):
  - Apoptosis of basal keratinocytes and epidermal edema
  - Dose-dependent effects ranging from erythema to desquamation (ie, skin peeling), superficial ulceration, and/or blistering
  - Pigment changes and loss of skin appendages (eg, hair follicles, sebaceous glands)
- Late (months to years after radiotherapy):



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- Pigment changes and loss of skin appendages (eg, hair follicles, sebaceous glands)
- Late (months to years after radiotherapy):
  - **Fibrosis**, characterized histologically by **homogenization of dermal collagen**, due to fibroblast activation by **transforming growth factor-beta** from damaged tissue and responding immune cells
  - Vascular damage, resulting in chronic hypoxia and ulceration
  - Abnormal, dilated microvasculature (ie, telangiectasias)

**(Choice A)** Full-thickness epidermal necrosis with **subepidermal bullae** is characteristic of Stevens-Johnson syndrome/toxic epidermal necrolysis. This systemic immune reaction to certain medications (eg, allopurinol, carbamazepine, sulfonamides) results in fever, skin tenderness, desquamation, and **widespread blistering**.

**(Choice C)** Neutrophilic infiltrates and **elongation of dermal papillae** are characteristic of psoriasis vulgaris, which typically causes symmetric, salmon-colored **scaly plaques** with sharply defined borders.

**(Choice D)** During an urticarial reaction, mast cells release inflammatory mediators and cytokines (eg, IL-5) that can recruit eosinophils, resulting in perivascular collections of eosinophils in and around the



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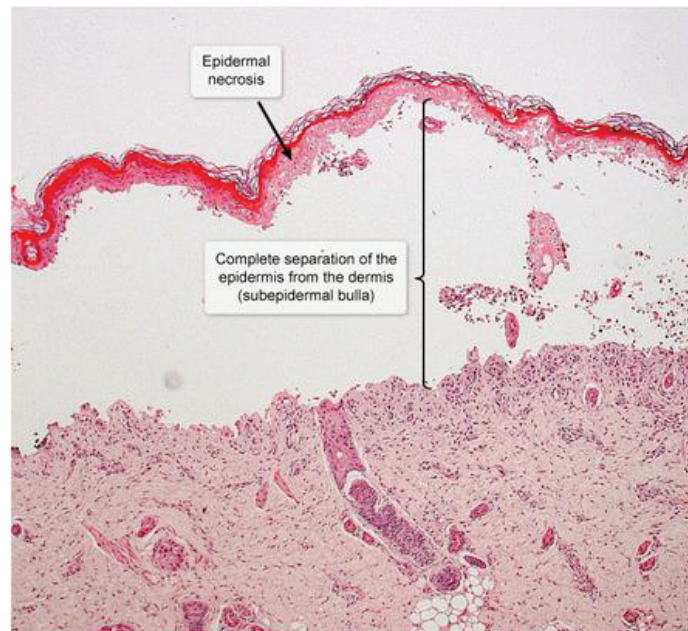
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Pigment changes and loss of skin appendages (eg. hair follicles, sebaceous glands)

## Exhibit Display

## Toxic epidermal necrolysis



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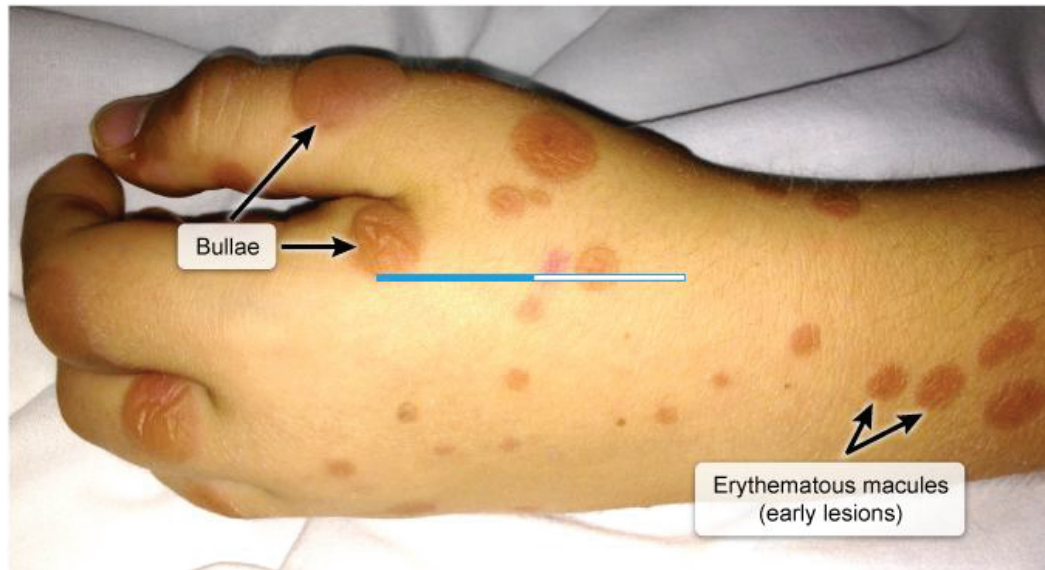
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Pigment changes and loss of skin appendages (eg. hair follicles, sebaceous glands)

Exhibit Display

### Toxic epidermal necrolysis



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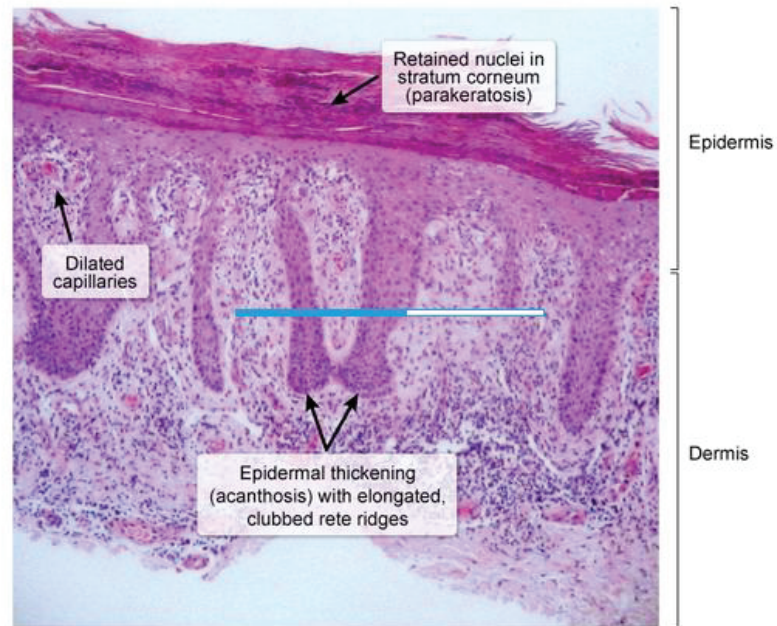
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Pigment changes and loss of skin appendages (eg. hair follicles, sebaceous glands)

## Exhibit Display

## Psoriasis



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Pigment changes and loss of skin appendages (eg. hair follicles, sebaceous glands)

## Exhibit Display

## Psoriasis



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allopurinol, carbamazepine, sulfonamides) results in fever, skin tenderness, desquamation, and **widespread blistering**.

**(Choice C)** Neutrophilic infiltrates and **elongation of dermal papillae** are characteristic of psoriasis vulgaris, which typically causes symmetric, salmon-colored **scaly plaques** with sharply defined borders.

**(Choice D)** During an urticarial reaction, mast cells release inflammatory mediators and cytokines (eg, IL-5) that can recruit eosinophils, resulting in perivascular collections of eosinophils in and around the urticarial lesion. Urticaria usually manifests as pruritic, erythematous plaques (ie, **wheal and flare reaction**).

### Educational objective:

Late-stage radiation dermatitis occurs months to years after radiation exposure and is characterized grossly by pigment changes, telangiectasias, and chronic ulceration. Typical histologic changes include vascular abnormalities, fibroblast proliferation, and homogenization of dermal collagen (ie, fibrosis) due to the increased expression of transforming growth factor-beta.

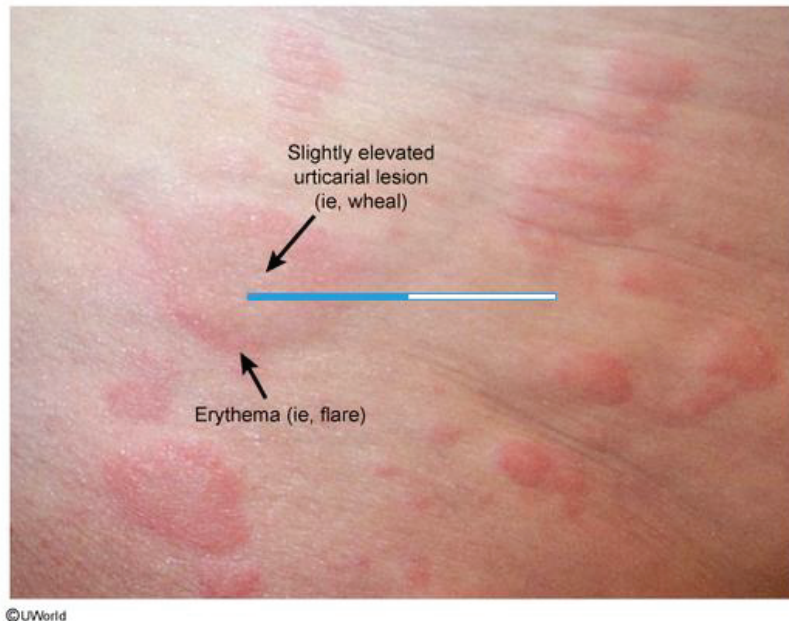
### References

- **Chronic radiation-induced dermatitis: challenges and solutions.**

Pathology      Dermatology      Radiation injury

### Exhibit Display

#### Wheal and flare



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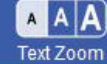
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 32-year-old woman comes to the allergy clinic due to a recurrent skin rash. The patient has had several episodes of itchy, erythematous, vesicular eruptions on her hands over the past several months. She works at a hair salon and is often exposed to hair dye and other beauty products. The patient has no other medical conditions and takes no medications. She undergoes patch testing, during which several allergens found in common cosmetic products are mounted on nonocclusive tape strips applied to her upper back. Skin findings developed after 2 days of application and are shown in the [exhibit](#). Which of the following processes most likely occurred in this patient to enable the development of the observed skin reaction?

- ☐ A. B-cell binding with helper T cells via CD40 and CD40 ligand
- ☐ B. Formation of autoantibodies against keratinocyte cell surface antigens
- ☐ C. Immune complex formation and deposition in the small cutaneous vessels
- ☐ D. Migration of hapten-activated Langerhans cells to regional lymph nodes
- ☐ E. Release of vasoactive peptides from IgE-bound mast cells

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Lab Values



Notes



Calculator



Reverse Color

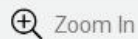
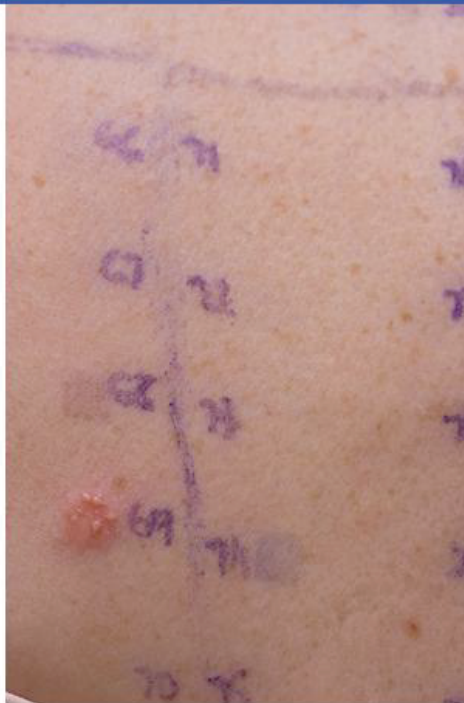


Text Zoom

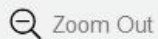


Settings

## Exhibit Display



Zoom In



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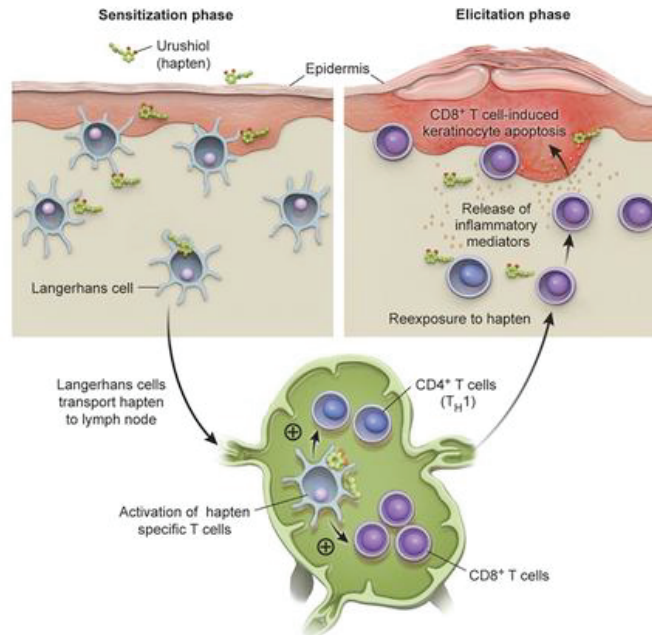
A 32-year-old woman comes to the allergy clinic due to a recurrent skin rash. The patient has had several episodes of itchy, erythematous, vesicular eruptions on her hands over the past several months. She works at a hair salon and is often exposed to hair dye and other beauty products. The patient has no other medical conditions and takes no medications. She undergoes patch testing, during which several allergens found in common cosmetic products are mounted on nonocclusive tape strips applied to her upper back. Skin findings developed after 2 days of application and are shown in the exhibit. Which of the following processes most likely occurred in this patient to enable the development of the observed skin reaction?

- ☐ A. B-cell binding with helper T cells via CD40 and CD40 ligand (28%)
- ☐ B. Formation of autoantibodies against keratinocyte cell surface antigens (3%)
- ☒ C. Immune complex formation and deposition in the small cutaneous vessels (5%)
- ☒ D. Migration of hapten-activated Langerhans cells to regional lymph nodes (43%)
- ☐ E. Release of vasoactive peptides from IgE-bound mast cells (19%)

Incorrect

### Exhibit Display

#### Urushiol-induced contact dermatitis



Zoom In

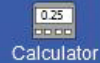
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This patient developed localized erythema and vesicles 2 days after reexposure to a chemical on patch testing, which identified the allergen responsible for **allergic contact dermatitis** (ACD). ACD is a type IV (**delayed-type**) hypersensitivity reaction that occurs in 2 phases:

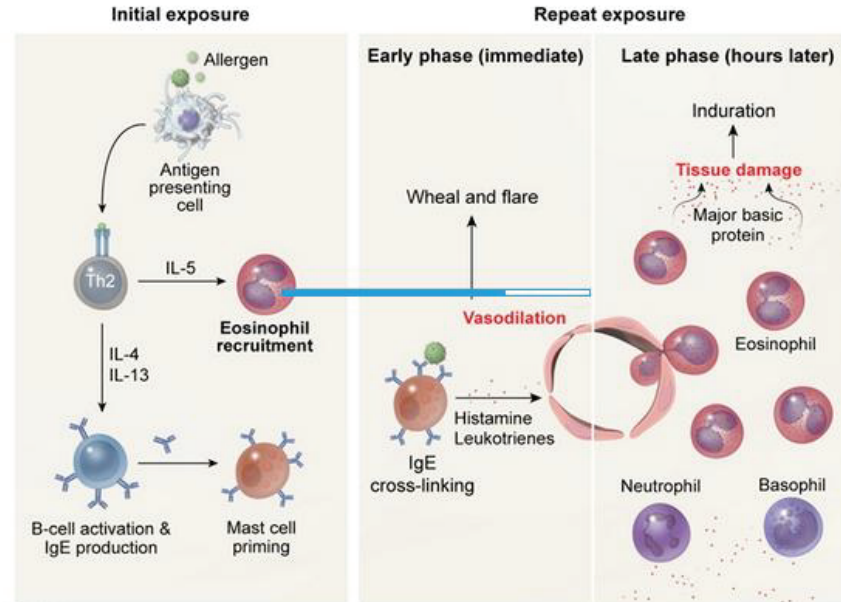
- In the **sensitization phase**, cutaneous **Langerhans cells** take up haptens (ie, allergens) and present them to naive CD4<sup>+</sup> and CD8<sup>+</sup> T cells in the regional lymph nodes, resulting in clonal expansion of hapten-sensitive T cells. This phase takes **10-14 days** and does not result in cutaneous lesions.
- On reexposure to the hapten, cutaneous antigen-presenting cells present the hapten to **sensitized T cells** recruited to the skin. When activated, these T cells mediate tissue damage that manifests as pruritic erythema, vesicles, and/or bullae. This **elicitation phase** occurs **2-3 days** following reexposure to the hapten.

**(Choices A and E)** In **type I (immediate) hypersensitivity** reactions, initial allergen exposure leads to Th2 cell-induced, B-cell heavy-chain isotype switching and production of IgE, which subsequently binds to mast cells. This is accomplished in part by the binding of CD40 on B cells to CD40 ligand on T cells. On reexposure, allergens bind to IgE on mast cells and trigger immediate release of vasoactive peptides, resulting in urticaria (and anaphylaxis if severe). This inflammatory response is rapid (ie, minutes), unlike



### Exhibit Display

#### Cutaneous type 1 hypersensitivity reactions



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resulting in urticaria (and anaphylaxis if severe). This inflammatory response is rapid (ie, minutes), unlike this patient's delayed (48-hr) response.

**(Choice B)** Bullous pemphigoid and pemphigus vulgaris are caused by autoantibodies against hemidesmosomes and desmosomes on keratinocytes, respectively. This causes epidermal/dermal separation and acantholysis, respectively, manifesting as **bullae**. These conditions are not hypersensitive reactions and cannot be elicited by patch testing.

**(Choice C)** Immune complex deposition in small cutaneous vessels causes cutaneous small vessel vasculitis (CSVV). Medications that function as haptens (eg, phenytoin, sulfonamides) can cause the condition. Because of the extravasation of red blood cells due to vessel wall inflammation, CSVV presents with nonblanchable **purpura and petechiae**, not vesicles.

### Educational objective:

Allergic contact dermatitis is a delayed-type hypersensitivity reaction. Initially, Langerhans cells travel to regional lymph nodes and present haptens to naive T cells, leading to clonal expansion. On reexposure to the hapten, sensitized T cells cause tissue destruction that manifests as pruritic erythema, vesicles, and/or bullae 2-3 days after exposure.

### References







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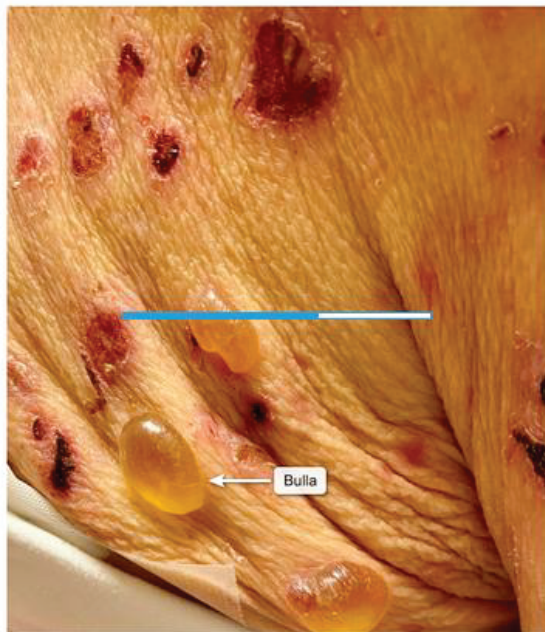
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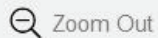
Bullous pemphigoid



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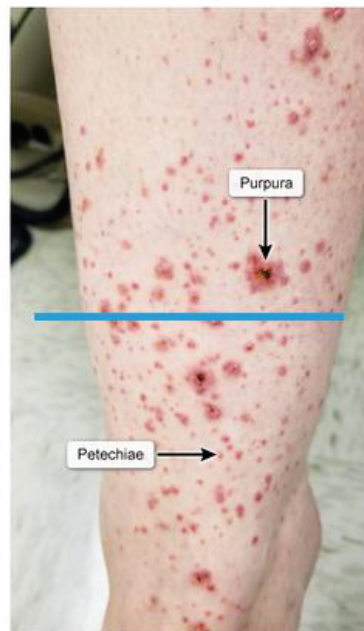


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## Exhibit Display

## Cutaneous small vessel vasculitis



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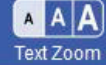
Notes



Calculator



Reverse Color



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Settings

A 56-year-old woman comes to the office due to a pigmented lesion on her back. She first noted the lesion a year ago and says it has enlarged. Past medical history is unremarkable. The patient has worked as a forest service ranger for the last 30 years and has spent much of her time outdoors. On examination, there is a large irregular pigmented lesion on the upper back, as shown in the [exhibit](#), as well as scattered patches of erythema and telangiectasias. Excisional biopsy of the lesion shows malignant melanoma. Which of the following is associated with the highest risk of metastasis for this patient's lesion?

- ☐ A. Active horizontal growth
- ☐ B. Active vertical growth
- ☐ C. Dense lymphocyte infiltration
- ☐ D. Multinucleated giant melanocytes
- ☐ E. Prominent cellular atypia

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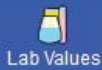
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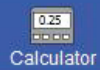
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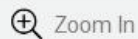


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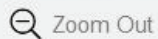


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Zoom In



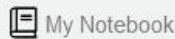
Zoom Out



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A 56-year-old woman comes to the office due to a pigmented lesion on her back. She first noted the lesion a year ago and says it has enlarged. Past medical history is unremarkable. The patient has worked as a forest service ranger for the last 30 years and has spent much of her time outdoors. On examination, there is a large irregular pigmented lesion on the upper back, as shown in the [exhibit](#), as well as scattered patches of erythema and telangiectasias. Excisional biopsy of the lesion shows malignant melanoma. Which of the following is associated with the highest risk of metastasis for this patient's lesion?

- ☐ A. Active horizontal growth (1%)
- ☒ B. Active vertical growth (91%)
- ☐ C. Dense lymphocyte infiltration (1%)
- ☐ D. Multinucleated giant melanocytes (0%)
- ☐ E. Prominent cellular atypia (4%)

Correct



91%

Answered correctly



35 secs

Time Spent



02/19/2021

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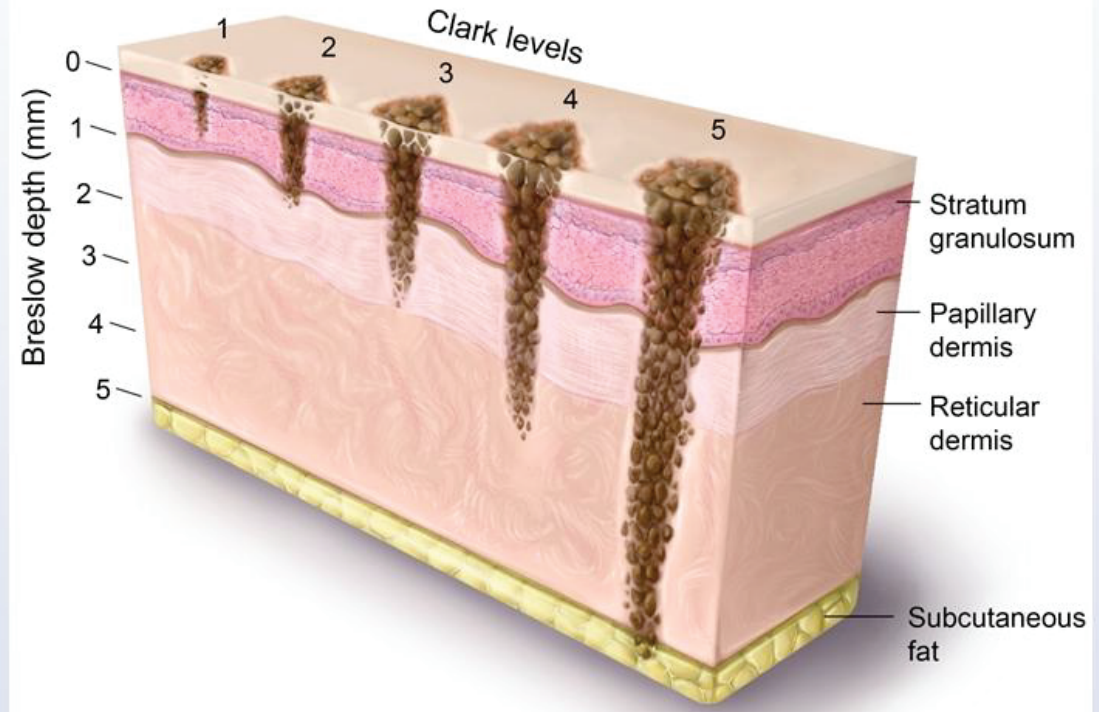


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## Melanoma depth of invasion







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**Malignant melanoma** most often arises in the skin, although it may occur wherever there are pigmented cells, such as the eye and the mucosa of the gastrointestinal tract. Sunlight exposure appears to be an important factor in the pathogenesis of dermal melanoma, as are hereditary factors and a history of preexistent dysplastic nevi. Light-skinned individuals are at greatest risk.

On gross inspection, **melanomas** are characterized by asymmetric shape, irregular or jagged border, variability of color (brown, black, red, blue, or unpigmented), diameter  $>0.5$  cm, and evolution in size and appearance over time (**ABCDE criteria**). Histologically, **melanoma cells** congregate in poorly formed nests and are large with irregular nuclei, clumped chromatin, and prominent nucleoli.

In early development, many melanomas exhibit a radial growth phase. This superficial, horizontal growth within the epidermis and superficial dermis carries a very low risk of metastatic spread (**Choice A**). In contrast, melanomas in the **vertical growth phase** contain melanoma cells that travel downward into the deeper dermal layers, **increasing metastatic risk**. Vertical growth often corresponds to a palpable nodularity of the lesion. The **Breslow depth** (distance from the epidermal granular cell layer to the deepest visible melanoma cells) is the most important prognostic indicator in malignant melanoma.

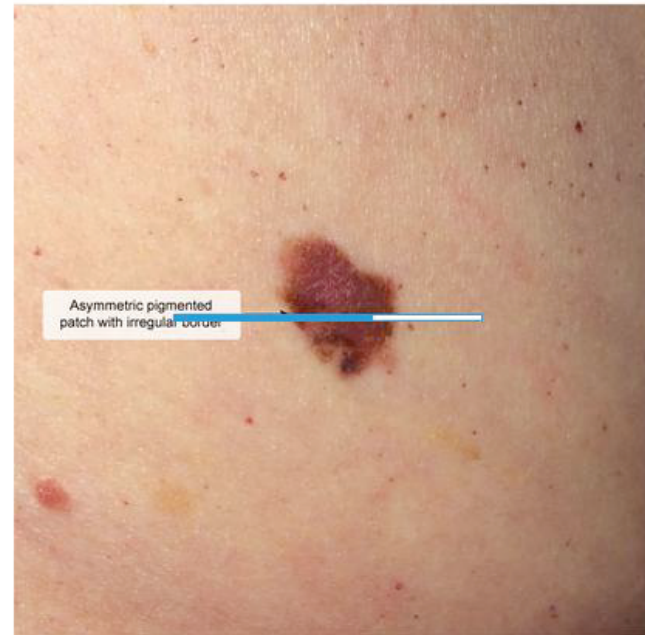
**(Choice C)** A dense lymphocytic infiltration of the tumor suggests a robust immune response and is thought to improve prognosis.



Malignant melanoma most often arises in the skin, although it may occur wherever there are pigmented

Exhibit Display

Melanoma



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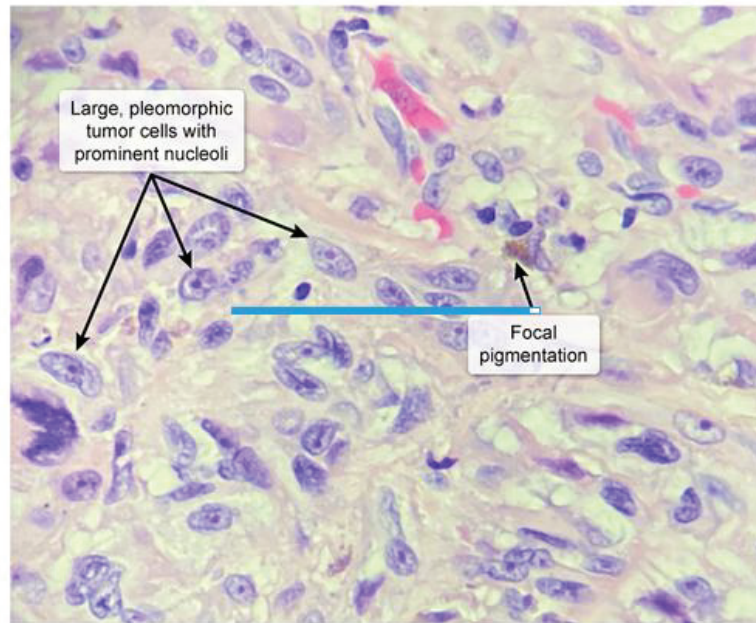
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Malignant melanoma most often arises in the skin, although it may occur wherever there are pigmented

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Melanoma



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Settings

**(Choice D)** Multinucleated giant melanocytes are a characteristic finding in lentigo maligna melanoma.

**Lentigo maligna** are common pigmented lesions in elderly patients and are considered to be a type of melanoma in-situ. When melanoma develops in lentigo maligna, the prognosis is similar to other melanomas of the same stage.

**(Choice E)** Prominent cellular atypia is a classic finding of malignant melanoma, but it is not considered the most important risk factor for metastatic disease.

### Educational objective:

Melanoma often has an early horizontal growth phase with low metastatic potential followed by a nodular, vertical growth phase with a significantly increased risk of metastasis. Depth of invasion (Breslow thickness) is the most important prognostic indicator in malignant melanoma.

### References

- [Thin melanoma.](#)

Pathology

Dermatology

Melanoma

Subject

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Topic

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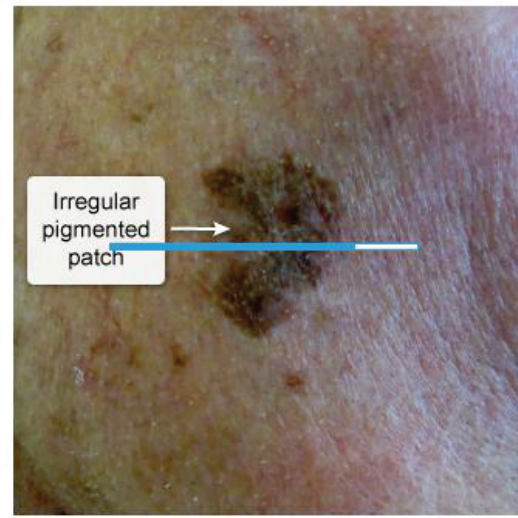
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Lentigo maligna



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Settings

A 2-month-old girl is brought to the office for a follow-up examination. The parents are concerned about a red bump that first appeared on her scalp at age 3 weeks. The lesion has since grown significantly in size. The child's growth and development are appropriate for age. A photograph of the lesion is shown in the [exhibit](#). Examination shows no other abnormalities. This child's lesion is most likely primarily composed of which of the following?

- ☐ A. Chondrocytes
- ☐ B. Endothelial cells
- ☐ C. Neuroendocrine cells
- ☐ D. Smooth muscle cells
- ☐ E. Squamous epithelial cells

**Submit**

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A 2-month-old girl is brought to the office for a follow-up examination. The parents are concerned about a red bump that first appeared on her scalp at age 3 weeks. The lesion has since grown significantly in size. The child's growth and development are appropriate for age. A photograph of the lesion is shown in the [exhibit](#). Examination shows no other abnormalities. This child's lesion is most likely primarily composed of which of the following?

- ☐ A. Chondrocytes (1%)
- ☒ B. Endothelial cells (77%)
- ☐ C. Neuroendocrine cells (7%)
- ☐ D. Smooth muscle cells (6%)
- ☐ E. Squamous epithelial cells (7%)

Correct



77%

Answered correctly



17 secs

Time Spent



10/14/2020

Last Updated



1



Feedback



Suspend



End Block

### Infantile hemangioma

<b>Pathology</b>	<ul style="list-style-type: none"><li>• Benign proliferation of endothelial cells</li><li>• Lobules of densely packed capillaries</li></ul>
<b>Natural history</b>	<ul style="list-style-type: none"><li>• Appears days to weeks after birth</li><li>• Proliferation in infancy<ul style="list-style-type: none"><li>◦ Bright red, raised plaques</li><li>◦ Soft, compressible, well-demarcated</li></ul></li><li>• Involution &amp; regression in size through early childhood</li></ul>
<b>Management</b>	<ul style="list-style-type: none"><li>• Observation if uncomplicated (ie, no ulceration or vision/airway obstruction)</li></ul>

This patient's rapidly growing lesion is consistent with an **infantile hemangioma**, a common, **benign vascular tumor** characterized by neoplastic proliferation of **endothelial cells**.

Infantile hemangiomas occur most often on the head or neck. They present within weeks of birth as a solitary red papule or nodule. The lesion shows characteristic **rapid growth** for several months followed by spontaneous, **gradual regression** over several years.





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spontaneous, **gradual regression** over several years.

Growth of infantile hemangiomas is thought to be related to the de novo production of a vascular network (ie, vasculogenesis) and/or the sprouting of new blood vessels from existing ones (ie, angiogenesis).

**Microscopic examination** during the growth phase shows multiple **lobules** of densely packed **capillaries** lined by plump endothelium. As the lesion regresses, the endothelial cells undergo apoptosis, and the capillaries are replaced by fibrofatty tissue.

**(Choice A)** Enchondroma and chondrosarcoma are examples of cartilage-forming neoplasms.

Enchondromas are benign and commonly involve the bones of the hands and feet. Chondrosarcomas are malignant lesions that usually involve the axial skeleton of older adults.

**(Choice C)** Merkel cell carcinoma is a rare, cutaneous tumor of neuroendocrine cell origin that presents as a rapidly expanding, firm, pink nodule. This condition is nearly exclusive to older adults.

**(Choice D)** Leiomyoma (benign) and leiomyosarcoma (malignant) are smooth muscle neoplasms most commonly found in the genitourinary (eg, uterus) or gastrointestinal tract. Lesions can involve the skin but present as small, painful nodules. In addition, these tumors are exceedingly rare in young children and do not grow rapidly.

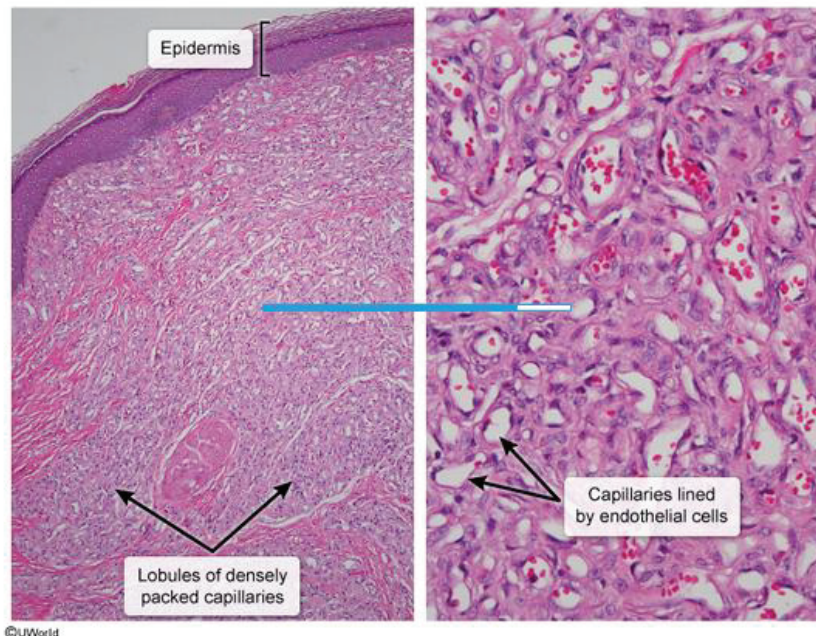
**(Choice E)** Squamous epithelial cells may give rise to **squamous cell carcinoma**, which, in contrast to this



spontaneous gradual regression over several years

## Exhibit Display

## Infantile hemangioma



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(Choice E) Squamous epithelial cells may give rise to squamous cell carcinoma, which, in contrast to this

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**(Choice D)** Leiomyoma (benign) and leiomyosarcoma (malignant) are smooth muscle neoplasms most commonly found in the genitourinary (eg, uterus) or gastrointestinal tract. Lesions can involve the skin but present as small, painful nodules. In addition, these tumors are exceedingly rare in young children and do not grow rapidly.

**(Choice E)** Squamous epithelial cells may give rise to [squamous cell carcinoma](#), which, in contrast to this case, appears as an ulcerated or hyperkeratotic plaque in adults with sun-damaged skin.

### Educational objective:

Infantile hemangiomas are benign vascular tumors composed of proliferating endothelial cells that most frequently affect the head or neck region. Natural history of these lesions involves rapid growth of a red, cutaneous plaque followed by spontaneous regression.

### References

- [Hemangioma.](#)

Pathology

Dermatology

Hemangioma

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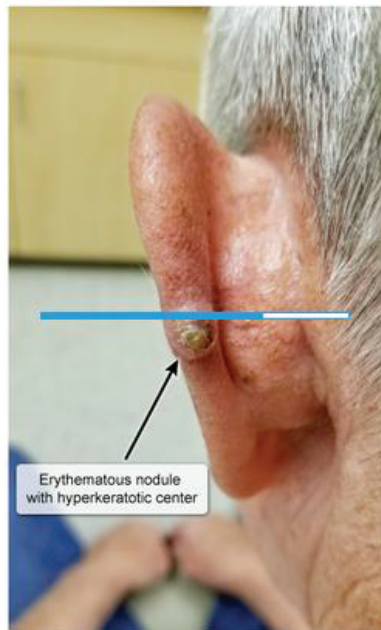
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(Choice D) Leiomyoma (benign) and leiomyosarcoma (malignant) are smooth muscle neoplasms most

## Exhibit Display

## Squamous cell carcinoma



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A 14-month-old girl is brought to the clinic by her parents due to sores on her feet. Since she took her first steps 3 months ago, she has had blisters involving the soles of the feet, which subsequently break down and heal slowly. The patient had failure to thrive as an infant due to frequent oral ulcerations but otherwise has been healthy and has achieved normal developmental milestones. Examination shows small bullae at the soles with faint erythema and no scarring. Biopsy taken at the margin of a blister shows an intraepidermal cleavage plane. Which of the following most likely contributes to the pathogenesis of this patient's condition?

- ☐ A. Autoantibodies against tissue transglutaminase
- ☐ B. Impaired keratin filament assembly
- ☐ C. Loss of function mutation in filaggrin
- ☐ D. T-cell-mediated hypersensitivity reaction

**Submit**

A 14-month-old girl is brought to the clinic by her parents due to sores on her feet. Since she took her first steps 3 months ago, she has had blisters involving the soles of the feet, which subsequently break down and heal slowly. The patient had failure to thrive as an infant due to frequent oral ulcerations but otherwise has been healthy and has achieved normal developmental milestones. Examination shows small bullae at the soles with faint erythema and no scarring. Biopsy taken at the margin of a blister shows an intraepidermal cleavage plane. Which of the following most likely contributes to the pathogenesis of this patient's condition?

- ☐ A. Autoantibodies against tissue transglutaminase (15%)
- ✓ ☐ B. Impaired keratin filament assembly (38%)
- ✗ ☒ C. Loss of function mutation in filaggrin (27%)
- ☐ D. T-cell-mediated hypersensitivity reaction (18%)

Incorrect

Correct answer  
B

38%  
Answered correctly

02 mins, 10 secs  
Time Spent

12/07/2020  
Last Updated



## Epidermolysis bullosa

<b>Etiology</b>	<ul style="list-style-type: none"><li>• Inherited disorders</li><li>• Mutations involving intraepidermal &amp; dermoepidermal adhesion complexes</li></ul>
<b>Clinical features</b>	<ul style="list-style-type: none"><li>• Onset in infancy/childhood</li><li>• Bullae, erosions &amp; ulcers</li><li>• Lesions triggered by friction or minor trauma</li><li>• Histopathology: intraepidermal cleavage most common</li></ul>
<b>Complications</b>	<ul style="list-style-type: none"><li>• Malnutrition</li><li>• Infection</li></ul>

**Epidermolysis bullosa (EB)** is a group of inherited disorders caused by mutations involving intraepidermal and dermoepidermal adhesion complexes in the basement membrane zone. It is characterized by epithelial fragility (eg, bullae, erosions, **ulcers**) triggered by minor trauma. Light microscopy of skin biopsy typically shows intraepidermal cleavage, although the plane of cleavage can vary based on subtype.

The most common form of EB, EB simplex, is caused by **mutations in keratin genes** that impair the assembly of keratin into filaments. It presents early in life with **friction-induced blisters** at the palms and

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The most common form of EB, EB simplex, is caused by **mutations in keratin genes** that impair the assembly of keratin into filaments. It presents early in life with **friction-induced blisters** at the palms and soles and other exposed areas. Lesions typically heal with no residual scarring, although patients may have chronic thickening of the skin of the feet. Infants with EB simplex may develop **oral blisters** with bottle-feeding.

**(Choice A)** Dermatitis herpetiformis is caused by autoantibodies against tissue transglutaminase. It presents with small, intensely pruritic vesicles on the elbows, knees, and buttocks and is typically seen in patients with gluten-sensitive enteropathy (ie, celiac disease).

**(Choice C)** Atopic dermatitis is a multifactorial disorder but is commonly seen in association with loss of function mutations in filaggrin and other epidermal barrier proteins. Infants have red, crusted lesions at the extensor surfaces and face, whereas older children and adults have pruritic patches and lichenification at flexural areas.

**(Choice D)** A delayed T-cell-mediated hypersensitivity reaction is responsible for allergic contact dermatitis (eg, poison ivy/rhus dermatitis), which presents acutely with pruritic vesicles at sites of contact.

**Educational objective:**

Epidermolysis bullosa is a group of inherited disorders characterized by epithelial fragility (eg, blisters).

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**(Choice A)** Dermatitis herpetiformis is caused by autoantibodies against tissue transglutaminase. It

presents with small, intensely pruritic vesicles on the elbows, knees, and buttocks and is typically seen in patients with gluten-sensitive enteropathy (ie, celiac disease).

**(Choice C)** Atopic dermatitis is a multifactorial disorder but is commonly seen in association with loss of function mutations in filaggrin and other epidermal barrier proteins. Infants have red, crusted lesions at the extensor surfaces and face, whereas older children and adults have pruritic patches and lichenification at flexural areas.

**(Choice D)** A delayed T-cell-mediated hypersensitivity reaction is responsible for allergic contact dermatitis (eg, poison ivy/rhus dermatitis), which presents acutely with pruritic vesicles at sites of contact.

### Educational objective:

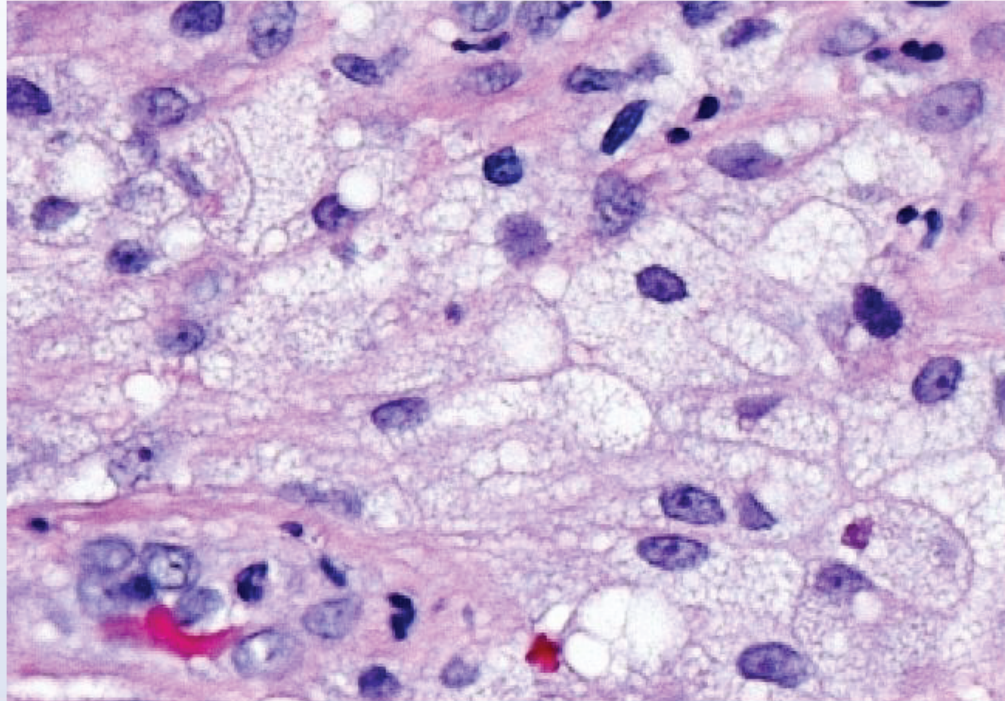
Epidermolysis bullosa is a group of inherited disorders characterized by epithelial fragility (eg, bullae, erosions, ulcers) triggered by minor trauma. It is caused by mutations affecting proteins in the intraepidermal and dermoepidermal adhesion complexes; keratin mutations are responsible for the most common form (EB simplex).

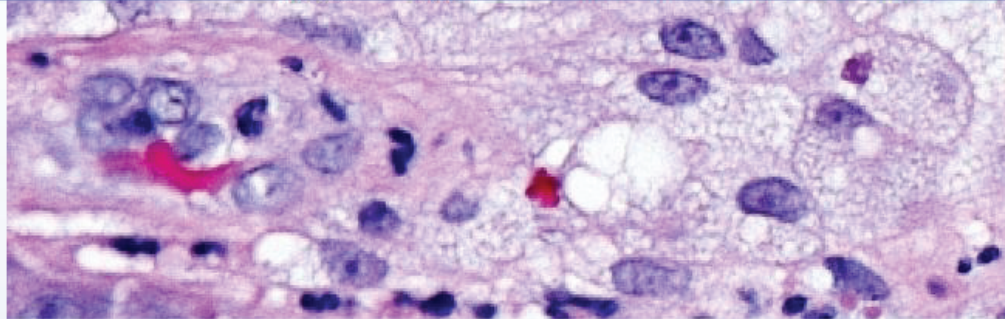
### References

- [Hereditary epidermolysis bullosa.](#)



A skin lesion on the upper eyelid of a 46-year-old woman is biopsied. Light microscopy of the tissue specimen is shown in the image below.

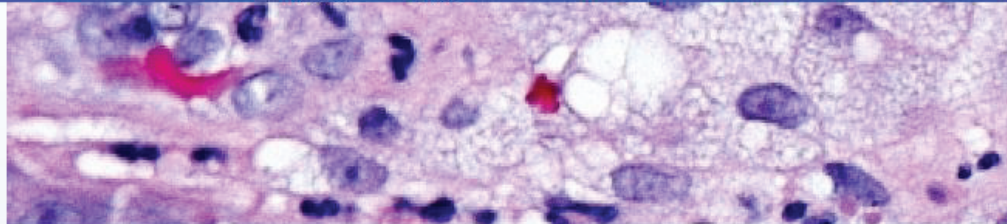




This lesion is most likely to be associated with which of the following conditions?

- ☐ A. Ankylosing spondylitis
- ☐ B. Hemochromatosis
- ☐ C. Hyperthyroidism
- ☐ D. Peptic ulcer disease
- ☐ E. Polycystic kidney disease
- ☐ F. Primary biliary cholangitis





This lesion is most likely to be associated with which of the following conditions?

- ☐ A. Ankylosing spondylitis (8%)
- ☐ B. Hemochromatosis (8%)
- ☐ C. Hyperthyroidism (20%)
- ☐ D. Peptic ulcer disease (2%)
- ☐ E. Polycystic kidney disease (7%)
- ☒ F. Primary biliary cholangitis (51%)

Correct

51%



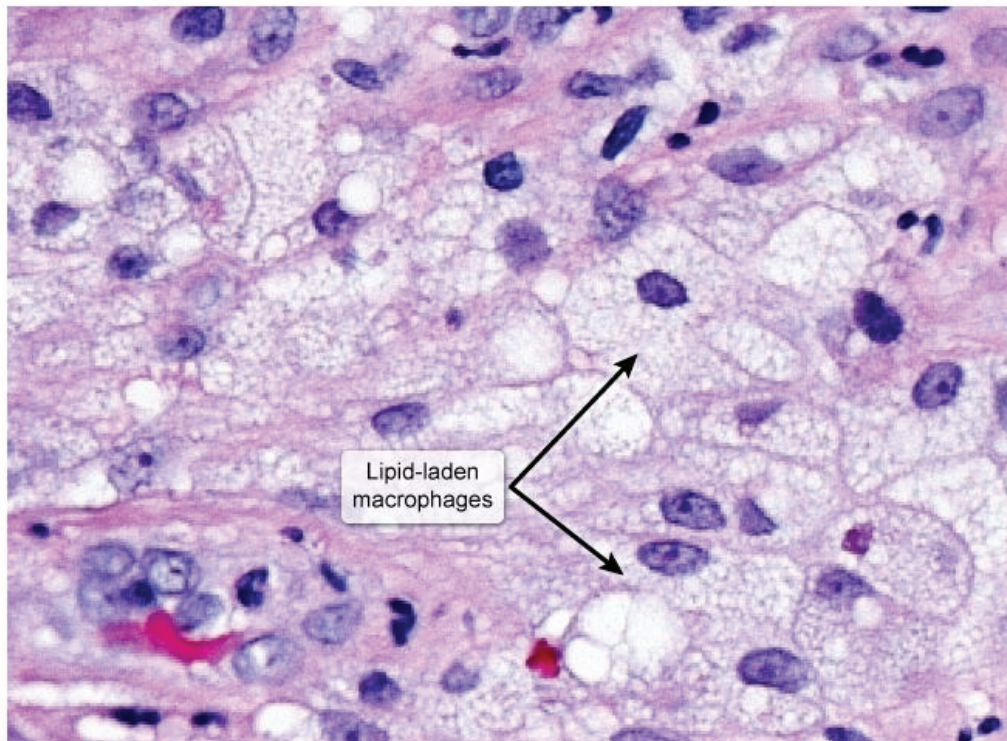
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03/11/2021



## Xanthelasma



Lipid-laden  
macrophages

**Xanthelasma** is a cutaneous lesion commonly found on the eyelid that contains **lipid-laden macrophages** (foam cells). These papules are typically **yellow** due to the location of the foam cells in the superficial dermis. Xanthelasma and other forms of xanthoma (tuberous, eruptive, tendinous) are classically associated with primary or secondary **hyperlipidemia**. Chronic cholestatic processes including obstructive biliary lesions and **primary biliary cholangitis** result in hypercholesterolemia due to leakage of bile back into the circulation, leading to the formation of xanthelasmas. Correction of underlying lipid defects can lead to slow resolution of these lesions.

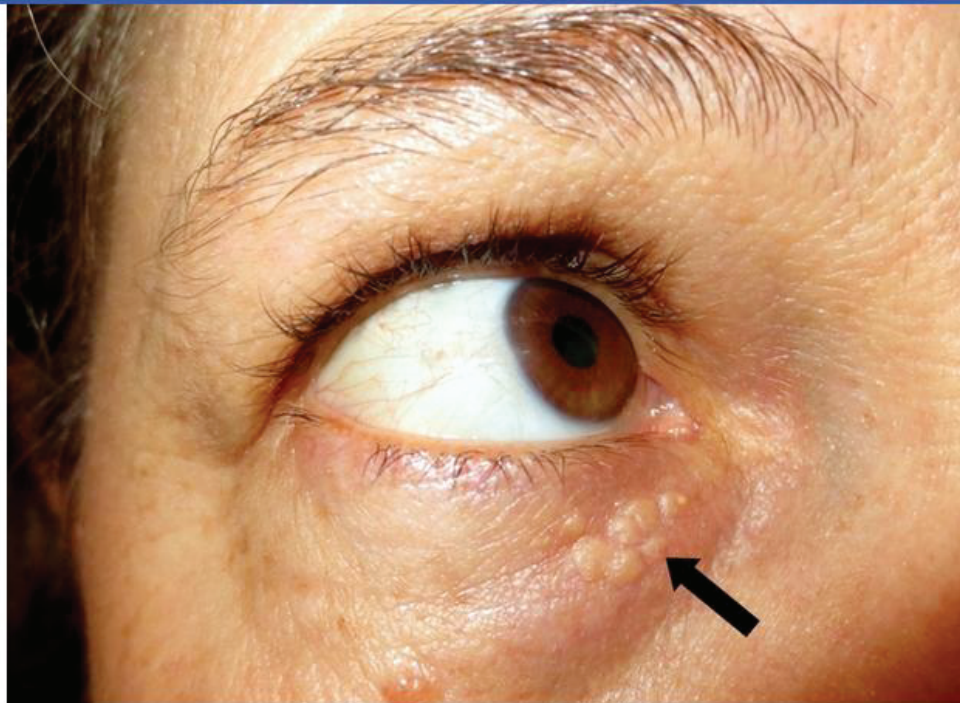
**(Choice A)** Ankylosing spondylitis is an HLA-B27-associated spondyloarthropathy that affects primarily young Caucasian males and causes debilitating pain and deformity of the spine and hips.

**(Choice B)** Hemochromatosis ("bronze diabetes") can cause generalized darkening of the skin due to hemosiderin deposition as well as cutaneous stigmata associated with chronic liver disease (eg, palmar erythema, gynecomastia, spider telangiectasias).

**(Choice C)** Graves' disease (the most common cause of hyperthyroidism) can present with pretibial myxedema and exophthalmos due to glycosaminoglycan accumulation. However, glycosaminoglycan accumulation occurs within the retroorbital space (not over the eyelids). In addition, hypothyroidism (not hyperthyroidism) is a common cause of hyperlipidemia.



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hyperthyroidism is a common cause of hyperlipidemia.



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erythema, gynecomastia, spider telangiectasias).

**(Choice C)** Graves' disease (the most common cause of hyperthyroidism) can present with pretibial myxedema and exophthalmos due to glycosaminoglycan accumulation. However, glycosaminoglycan accumulation occurs within the retroorbital space (not over the eyelids). In addition, hypothyroidism (not hyperthyroidism) is a common cause of hyperlipidemia.

**(Choice D)** Peptic ulcer disease may occur in multiple endocrine neoplasia 1.

**(Choice E)** Autosomal dominant polycystic kidney disease causes mild persistent proteinuria that can result in dyslipidemia. However, this is a less common cause of xanthelasma than biliary cirrhosis.

### Educational objective:

A yellowish eyelid papule or plaque containing lipid-laden macrophages is most likely xanthelasma. Xanthelasma may occur in association with primary or secondary hyperlipidemia. Cholestatic conditions such as primary biliary cholangitis are a potential cause of hypercholesterolemia leading to xanthelasma.

Pathology  
Subject

Dermatology  
System

Primary biliary cholangitis  
Topic

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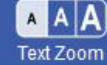
Notes



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Settings

A 4-month-old girl is brought to the clinic by her parents for a well-child check. She was evaluated 2 weeks ago for a rash in the diaper area. At that visit, the patient was found to have erythematous papules in the diaper area that spared the skin folds. Her symptoms improved with use of a petrolatum barrier ointment with every diaper change. Today, vital signs and physical examination are normal. Which of the following most likely contributed to this patient's prior skin findings?

- ☐ A. Abnormal keratin expression
- ☐ B. Altered local skin pH
- ☐ C. Increased hapten sensitization
- ☐ D. Local bacterial colonization
- ☐ E. Mite infestation

**Submit**





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Settings

A 4-month-old girl is brought to the clinic by her parents for a well-child check. She was evaluated 2 weeks ago for a rash in the diaper area. At that visit, the patient was found to have erythematous papules in the diaper area that spared the skin folds. Her symptoms improved with use of a petrolatum barrier ointment with every diaper change. Today, vital signs and physical examination are normal. Which of the following most likely contributed to this patient's prior skin findings?

- ☒ A. Abnormal keratin expression (10%)
- ☒ B. Altered local skin pH (42%)
- ☐ C. Increased hapten sensitization (32%)
- ☐ D. Local bacterial colonization (11%)
- ☐ E. Mite infestation (2%)

Incorrect

Correct answer

B



42%

Answered correctly



01 min, 53 secs

Time Spent



02/25/2021

Last Updated

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### Irritant diaper dermatitis





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Settings

This patient's rash that resolved with use of a barrier ointment was likely **irritant contact diaper dermatitis**, the most **common** diaper rash in infants. Characteristic features include erythematous papules confined within the diaper area. In contrast to **candidal diaper dermatitis**, another common diaper rash caused by a secondary yeast infection, irritant contact diaper dermatitis does not have skinfold involvement or satellite lesions (ie, discrete lesions beyond the borders of the main rash).

Irritant contact diaper dermatitis is predominantly caused by **skin barrier breakdown** from exposure to urine and stool trapped within the diaper. Patients with frequent stooling (eg, diarrhea) are at increased risk because urease produced by **fecal bacteria** causes an **increase in local skin pH**, which allows for activation of proteolytic enzymes that disrupt the stratum corneum. Areas of macerated skin are then prone to frictional damage from the diaper, which further exacerbates the rash.

The **treatment** for irritant contact diaper dermatitis is a thick **barrier ointment** (eg, petrolatum) or paste (eg, zinc oxide), which provides the skin an adherent layer of protection from contact with the stool and urine. Other measures to reduce irritant exposure include frequent diaper changes and diaper-free periods.

**(Choice A)** Abnormal keratin expression describes the pathogenesis of psoriasis, which manifests as erythematous, scaly plaques. Psoriasis rarely presents in the diaper area and is usually chronic and



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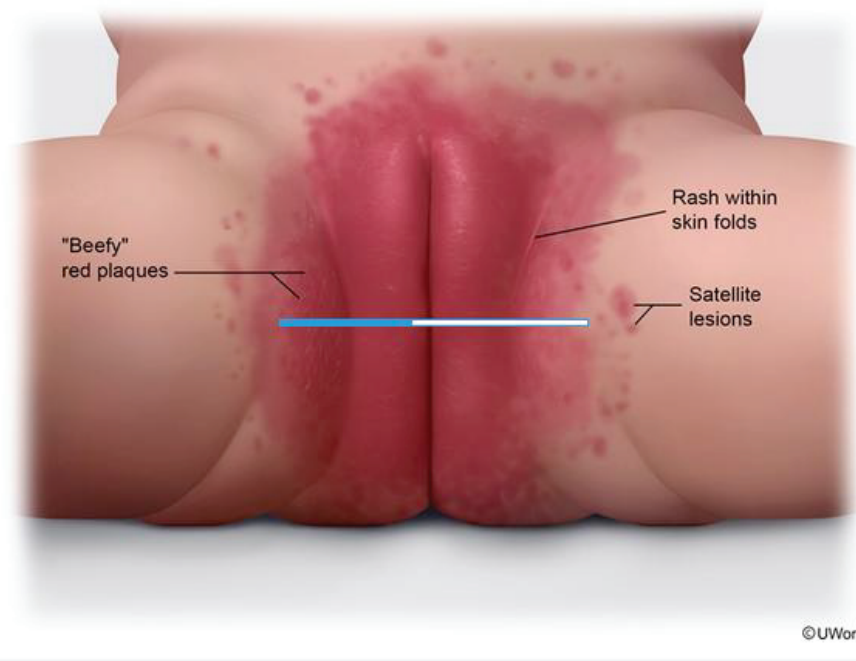
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This patient's rash that resolved with use of a barrier ointment was likely irritant contact dermatitis

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Candidal diaper dermatitis



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**(Choice A)** Abnormal keratin expression describes the pathogenesis of psoriasis, which manifests as erythematous, scaly plaques. Psoriasis rarely presents in the diaper area and is usually chronic and persistent without topical corticosteroid treatment.

**(Choice C)** Increased hapten sensitization describes allergic contact dermatitis, which is uncommon in the diaper area but can occur with an allergy to a component (eg, dye, fragrance) in diapers or wipes. The rash is unlikely to resolve without complete removal of the offending antigen (eg, changing diaper brand), and topical corticosteroids are also required in many cases.

**(Choice D)** Local bacterial colonization with *Staphylococcus* or *Streptococcus* leads to impetigo in the diaper area. Honey-crusted pustules are classic, and topical antibiotics are the first-line treatment.

**(Choice E)** Scabies is a mite infestation that causes itchy, erythematous papules. The rash can involve the diaper area, but lesions would also be expected elsewhere (eg, axillae, hands, feet). Treatment is with permethrin, and resolution would not be expected with petrolatum alone.

**Educational objective:**

Irritant contact diaper dermatitis is the most common diaper rash and is characterized by skin barrier breakdown as a result of exposure to fecal bacteria that causes increased local skin pH. Treatment is with a barrier ointment that prevents skin contact with urine and stool.



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**(Choice C)** Increased napten sensitization describes allergic contact dermatitis, which is uncommon in the diaper area but can occur with an allergy to a component (eg, dye, fragrance) in diapers or wipes. The rash is unlikely to resolve without complete removal of the offending antigen (eg, changing diaper brand), and topical corticosteroids are also required in many cases.

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### Educational objective:

Irritant contact diaper dermatitis is the most common diaper rash and is characterized by skin barrier breakdown as a result of exposure to fecal bacteria that causes increased local skin pH. Treatment is with a barrier ointment that prevents skin contact with urine and stool.

Pathophysiology

Dermatology

Diaper dermatitis

Subject

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Topic







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Settings

A 53-year-old woman comes to the clinic due to a skin rash. For the last 3 weeks, she has had a pruritic rash of worsening severity involving the posterior thighs. The patient recently began an exercise program to lose weight and has been applying a topical analgesic cream to her thighs and buttocks after her workouts. Her past medical history is unremarkable, and she does not use tobacco, alcohol, or illicit drugs. On physical examination, there is an erythematous rash with blisters, ulcers, and weeping drainage involving the posterior thighs bilaterally, as shown in the image below.



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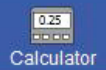
Tutorial



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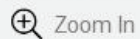


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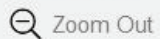


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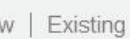
Zoom Out



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Feedback



Suspend



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Which of the following is the most likely finding on skin biopsy?

- ☐ A. Acanthosis
- ☐ B. Dyskeratosis
- ☐ C. Hypergranulosis
- ☐ D. Hyperkeratosis
- ☐ E. Spongiosis

Submit





Which of the following is the most likely finding on skin biopsy?

- ☐ A. Acanthosis (16%)
- ☐ B. Dyskeratosis (22%)
- ☐ C. Hypergranulosis (8%)
- ☐ D. Hyperkeratosis (7%)
- ☒ E. Spongiosis (44%)

Correct

44%



01 min, 13 secs



12/18/2020





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Settings

**Eczematous dermatitis** (eczema) is a group of conditions characterized by erythematous, papulovesicular, weeping lesions. This patient has **acute allergic contact dermatitis** (ACD), a form of eczema caused by a **type IV (delayed) hypersensitivity** reaction to an antigen on the skin surface. In ACD, antigens are taken up by antigen-presenting Langerhans cells and presented to CD4+ T cells in regional lymph nodes. The T cells are activated and migrate to the skin, where they incite an inflammatory response within 24 hours of antigen re-exposure.

Acute eczematous dermatitis is characterized histologically by **spongiosis**, an accumulation of **edema fluid** in the intercellular spaces of the **epidermis**. The intercellular bridges become more distinctive in an edematous background, and the epidermis is often described as "spongy." Eventually, the edema can become so marked as to form intraepidermal vesicles. A perivascular infiltrate of lymphocytes and eosinophils may also be seen; this may involve only the superficial dermis (if due to exposure to a surface antigen) or extend to include the deeper vessels (if due to a systemic antigen exposure [eg, drugs]).

With persistent antigen exposure, lesions may become less edematous and weepy. Thickening of the stratum spinosum (acanthosis) and stratum corneum (hyperkeratosis) produces raised, scaly **plaques** (Choices A and D).

(Choice B) Dyskeratosis is abnormal, premature keratinization of individual keratinocytes below the



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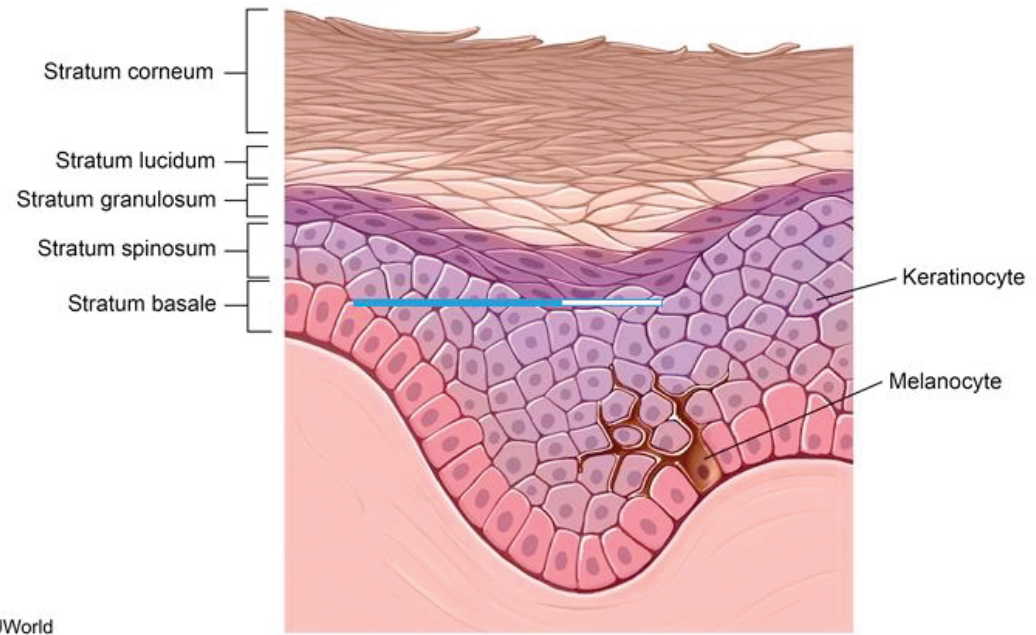
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### Exhibit Display

#### Epidermis of the skin



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stratum spinosum (acanthosis) and stratum corneum (hyperkeratosis) produces raised, scaly plaques (Choices A and D).

**(Choice B)** Dyskeratosis is abnormal, premature keratinization of individual keratinocytes below the stratum granulosum. Dyskeratosis can be due to genetic mutations (dyskeratosis congenita) or may be found in diseases such as squamous cell carcinoma.

**(Choice C)** Hypergranulosis is increased thickness of the stratum granulosum of the epidermis and is seen in conditions such as lichen planus.

### Educational objective:

Acute allergic contact dermatitis is caused by a type IV (delayed) hypersensitivity reaction to an antigen on the skin surface. Gross findings include erythematous, papulovesicular, weeping lesions. Histology is characterized by spongiosis, an accumulation of edema fluid in the intercellular spaces of the epidermis. With chronic exposure, lesions become less edematous, with thickening of the stratum spinosum and stratum corneum.

Pathology

Dermatology

Contact dermatitis

Subject

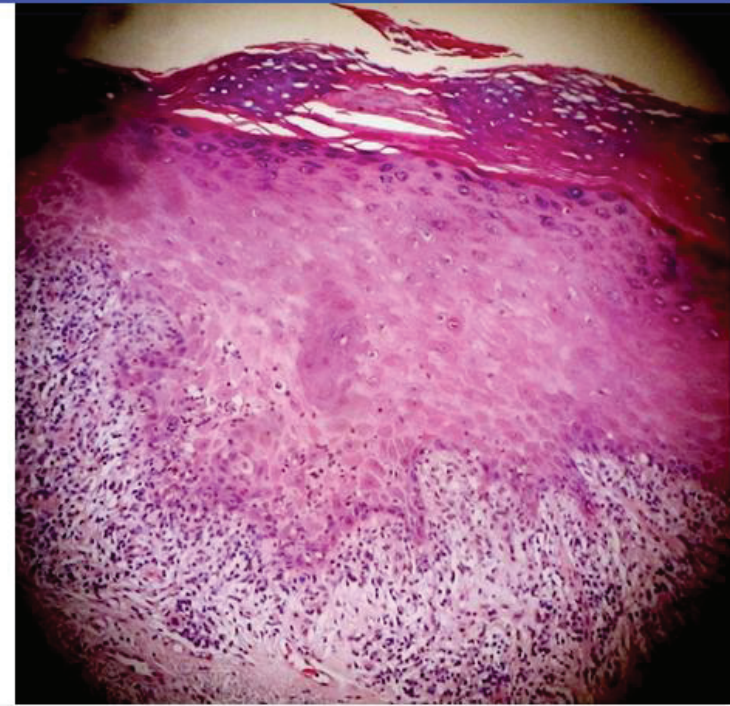
System

Topic



stratum spinosum (acanthosis) and stratum corneum (hyperkeratosis) produces raised, scaly

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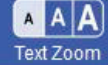
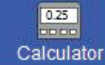
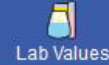




A 54-year-old woman comes to the physician because of multiple firm violaceous nodules on her right upper arm. She was diagnosed with right-sided breast carcinoma twelve years ago and was treated with radical mastectomy. Extensive axillary lymph node dissection performed at that time revealed no lymph node metastases. Post-operatively, the patient developed chronic lymphedema involving her right arm. Which of the following is the most likely etiology of her current skin lesions?

- ☐ A. Venous thrombosis
- ☐ B. Angiosarcoma
- ☐ C. Metastatic breast cancer
- ☐ D. Neurofibromas
- ☐ E. Cavernous hemangiomas

**Submit**



A 54-year-old woman comes to the physician because of multiple firm violaceous nodules on her right upper arm. She was diagnosed with right-sided breast carcinoma twelve years ago and was treated with radical mastectomy. Extensive axillary lymph node dissection performed at that time revealed no lymph node metastases. Post-operatively, the patient developed chronic lymphedema involving her right arm. Which of the following is the most likely etiology of her current skin lesions?

- ☐ A. Venous thrombosis (19%)
- ☒ B. Angiosarcoma (46%)
- ☐ C. Metastatic breast cancer (10%)
- ☐ D. Neurofibromas (5%)
- ☐ E. Cavernous hemangiomas (18%)

Correct

46%  
Answered correctly

45 secs  
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Chronic lymphedema is a risk factor for the development of cutaneous angiosarcoma, also known as Stewart-Treves syndrome. Radical mastectomy with axillary lymph node dissection is a classic predisposing procedure, although any form of chronic lymphedema can be implicated. Histopathologically, angiosarcoma will show infiltration of the dermis with slit-like abnormal vascular spaces. The prognosis for patients with angiosarcoma is poor because the tumor is usually widespread by the time of diagnosis. There is controversy regarding use of the term angiosarcoma versus lymphangiosarcoma, as it appears that this entity arises from blood vessels rather than from lymphatic vessels.

**(Choice A)** Thrombosis of the subclavian or axillary vein most frequently occurs as a complication of a chronic indwelling catheter.

**(Choice C)** Metastatic breast cancer is most likely to travel to bone, liver, and lung tissue. While it can have cutaneous metastases (usually affecting the anterior chest wall), the absence of lymphatic metastases on initial lymph node dissection makes this diagnosis less likely in this patient.

**(Choice D)** Neurofibromas are soft, rubbery, asymptomatic cutaneous nodules that commonly appear during the second and third decades of life.

**(Choice E)** Hemangiomas are benign congenital vascular neoplasms that affect infants. Hemangiomas





**(Choice C)** Metastatic breast cancer is most likely to travel to bone, liver, and lung tissue. While it can have cutaneous metastases (usually affecting the anterior chest wall), the absence of lymphatic metastases on initial lymph node dissection makes this diagnosis less likely in this patient.

**(Choice D)** Neurofibromas are soft, rubbery, asymptomatic cutaneous nodules that commonly appear during the second and third decades of life.

**(Choice E)** Hemangiomas are benign congenital vascular neoplasms that affect infants. Hemangiomas often enlarge in the months following birth before spontaneously involuting. A cavernous hemangioma is a deep hemangioma.

### Educational objective:

Axillary lymph node dissection is a risk factor for the development of chronic lymphedema involving the ipsilateral arm. Chronic lymphedema predisposes to the development of angiosarcoma (Stewart-Treves syndrome).

### References

- MRI of angiosarcoma associated with chronic lymphoedema: Stewart Treves syndrome.
- Images in clinical medicine. The Stewart-Treves syndrome.

A 17-year-old boy comes to the office for evaluation of a rash. For the past 2 years, the patient has had recurrent skin bumps that are frequently red and painful. He has no other medical conditions and takes no medications. Vital signs are within normal limits. Skin examination findings are shown below.





This patient's skin condition primarily affects which of the following structures?

- ☐ A. Dermal papillae
- ☐ B. Eccrine sweat glands
- ☐ C. Epidermal-dermal junction
- ☐ D. Melanocytes
- ☐ E. Pilosebaceous follicles
- ☐ F. Subcutaneous adipose tissue





This patient's skin condition primarily affects which of the following structures?

- ☐ A. Dermal papillae (5%)
- ☐ B. Eccrine sweat glands (7%)
- ☐ C. Epidermal-dermal junction (3%)
- ☐ D. Melanocytes (0%)
- ☒ E. Pilosebaceous follicles (82%)
- ☐ F. Subcutaneous adipose tissue (1%)

Correct

82%



28 secs



09/19/2020

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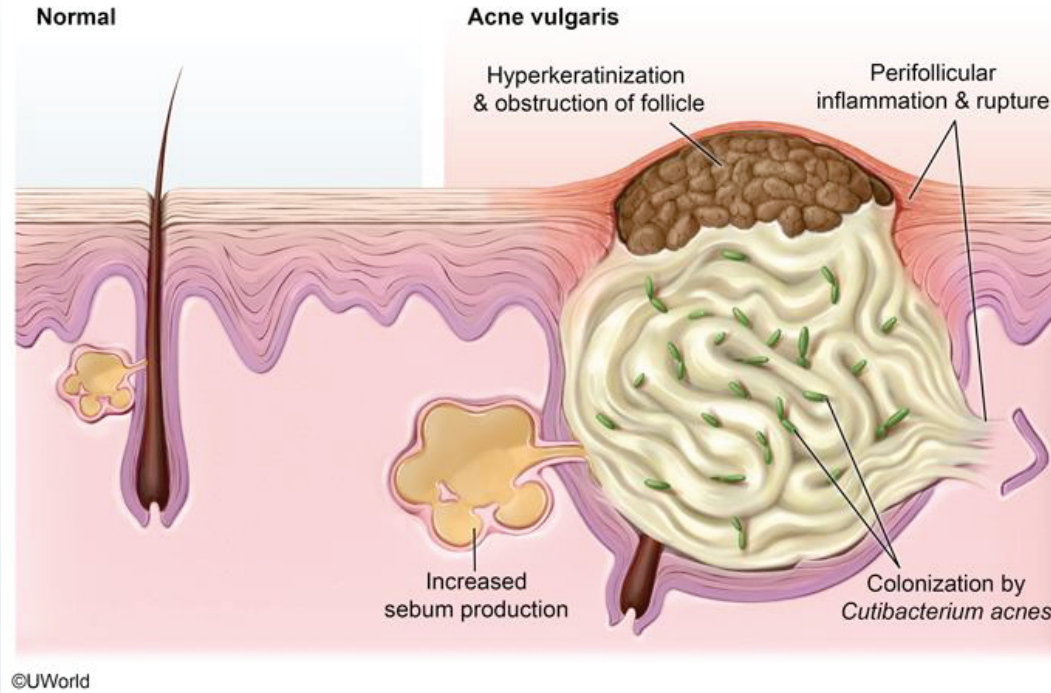


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## Pathogenesis of acne





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This patient has typical features of **acne vulgaris**. Acne usually appears in adolescence and can present with a variety of lesions, including **comedones**, papules, pustules, or inflammatory nodules, often with lesions in different stages concurrently. Nodular (sometimes called nodulocystic) acne, as in this patient, is often painful, difficult to treat, and can lead to the formation of sinus tracts and residual scarring.

Acne vulgaris is characterized by **inflammation of pilosebaceous follicles**. Contributing factors include **hyperkeratinization** and obstruction of follicles; sebaceous gland enlargement with **increased sebum secretion**; colonization of the gland by *Propionibacterium* (***Cutibacterium***) **acnes**, which metabolizes lipids in sebum and produces proinflammatory factors; and follicular and perifollicular inflammation with follicular rupture.

**(Choice A)** Dermatitis herpetiformis most commonly occurs in patients with celiac disease and is characterized by microabscesses containing fibrin and neutrophils at the dermal papillae tips. Clinical manifestations include pruritic papules, vesicles, and bullae that appear symmetrically on the extensor surfaces (eg, elbows, knees), upper back, and buttocks.

**(Choice B)** Eccrine sweat glands produce watery sweat in response to exertion, high ambient temperature, and emotional stress. The secretions from eccrine glands have little lipid content and do not support heavy colonization by *P. acnes*; therefore, these glands do not have a prominent role in the



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support heavy colonization by *P. acnes*; therefore, these glands do not have a prominent role in the

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support heavy colonization by *P. acnes*; therefore, these glands do not have a prominent role in the pathogenesis of acne.

**(Choice C)** Bullous pemphigoid is characterized by an autoimmune process that causes the epidermis to separate from the dermis, forming subepidermal blisters. It presents with tense, fluid-filled bullae on the inner thighs, forearms, axillae, groin, and abdomen.

**(Choice D)** Melanocyte disorders typically present with hyperpigmentation (eg, *melasma*) or hypopigmentation (eg, *vitiligo*).

**(Choice F)** Erythema nodosum—characterized by painful, subcutaneous nodules, typically in the lower legs—is a form of panniculitis (inflammation of the subcutaneous adipose tissue) caused by a delayed hypersensitivity reaction to antigens associated with various conditions (eg, herpes simplex).

### Educational objective:

Acne vulgaris is an inflammatory disorder of pilosebaceous follicles. Contributing factors include hyperkeratinization and obstruction of follicles; sebaceous gland enlargement with increased secretion of sebum; colonization and proliferation in the gland by *Propionibacterium (Cutibacterium) acnes*; and follicular and perifollicular inflammation.

### References





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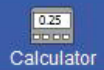
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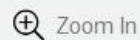


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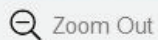


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## References

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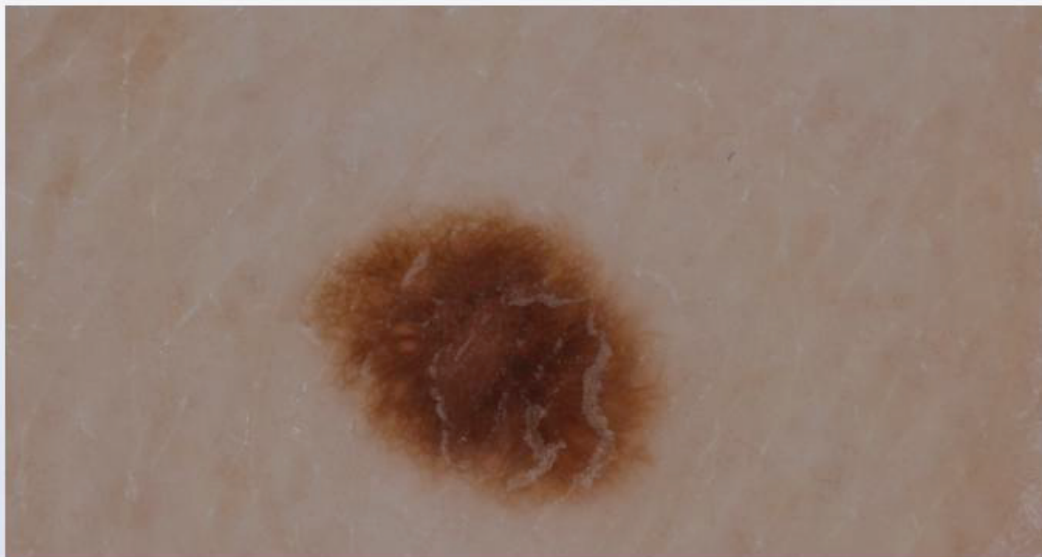


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A 28-year-old previously healthy woman comes to the office for evaluation of a raised, pigmented skin lesion on her leg. The patient has had no itching or pain and cannot remember how long she has had the lesion. She has used tanning machines a few times in the past but denies excessive sun exposure. She is particularly concerned about the risk of malignancy as her father was recently diagnosed with skin cancer. Skin examination shows the nodule seen in the image below.





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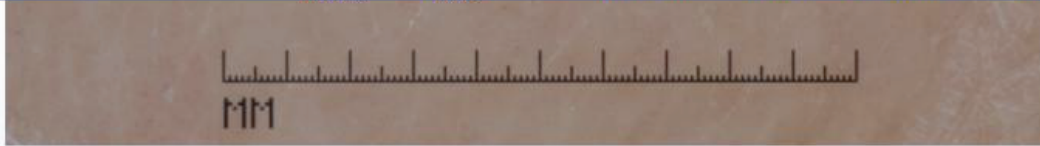
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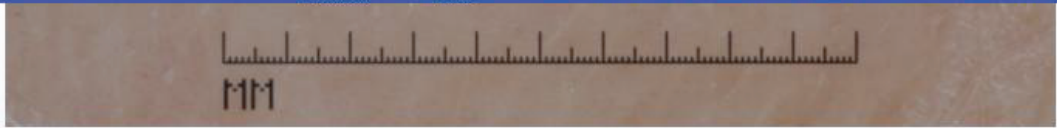


A biopsy of the lesion reveals nests of uniform round cells at the basal portion of the epidermis that extend into the underlying dermis. The cells contain inconspicuous nucleoli and show no mitotic activity. Which of the following is the most likely diagnosis?

- ☐ A. Atypical skin mole
- ☐ B. Compound melanocytic nevus
- ☐ C. Junctional nevus
- ☐ D. Malignant melanoma
- ☐ E. Pigmented basal cell carcinoma
- ☐ F. Seborrheic keratosis

**Submit**





A biopsy of the lesion reveals nests of uniform round cells at the basal portion of the epidermis that extend into the underlying dermis. The cells contain inconspicuous nucleoli and show no mitotic activity. Which of the following is the most likely diagnosis?

- ☐ A. Atypical skin mole (5%)
- ☒ B. Compound melanocytic nevus (40%)
- ☐ C. Junctional nevus (35%)
- ☐ D. Malignant melanoma (10%)
- ☐ E. Pigmented basal cell carcinoma (4%)
- ☐ F. Seborrheic keratosis (2%)

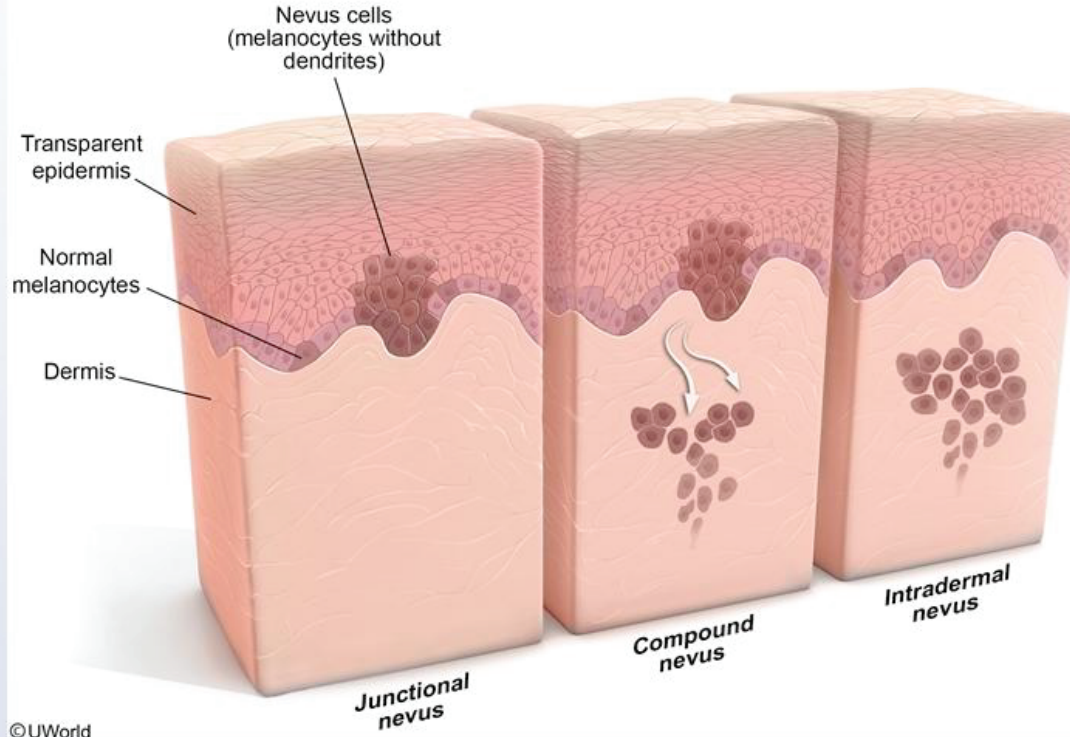
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Time Spent

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## Histology of nevi





Melanocytic nevi are benign neoplasms composed of round, uniform melanocytes (nevus cells) that are mitotically quiescent. They are typically  $\leq 6$  mm in diameter, and have a regular outline with a symmetrical, sharply demarcated border and a homogenous surface. Melanocytic nevi are progressive lesions that typically mature through the following phases:

1. **Junctional nevi** are characterized by aggregates of nevus cells limited to the dermoepidermal junction (**Choice C**). They typically appear as flat, black- to brown-pigmented macules with darker coloration in the center than the periphery and preserved skin markings.
2. **Compound nevi** form as the aggregates of nevus cells extend into the dermis. Compound nevi are raised papules with uniform brown to tan pigmentation. This patient's lesion is a compound nevus as it has **both dermal** and **epidermal** involvement.
3. **Intradermal nevi** are considered to be older lesions in which the epidermal nests of nevus cells have been lost. The remaining dermal nevus cells lose tyrosinase activity and produce little to no pigment. Intradermal nevi are skin- to tan-colored, dome-shaped, and sometimes pedunculated.

(**Choices A and D**) **Malignant melanoma** is characterized by irregular and asymmetrical borders with variable coloration, diameter  $> 5$  mm, and evolution over time. Melanomas typically expand superficially at first but may extend vertically into the dermis and subcutaneous tissues, extending a great distance





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**(Choices A and D)** **Malignant melanoma** is characterized by irregular and asymmetrical borders with variable coloration, diameter >5 mm, and evolution over time. Melanomas typically expand superficially at first but may extend vertically into the dermis and subcutaneous tissues, portending a poor prognosis. Compared to nevus cells, **melanoma cells** are larger, contain larger nuclei with prominent nucleoli, and have greater mitotic activity. **Atypical (dysplastic) nevi** can resemble melanoma but typically have less extreme features. The melanocytes commonly show cellular atypia and form coalescing nests that may fuse into a continuous layer at the dermoepidermal border.

**(Choice E)** **Pigmented basal cell carcinoma** can present as papules, nodules, or plaques with rolled borders on sun-exposed areas. They can have varying degrees of pigmentation due to functional melanocytes within the lesion. The **tumor cells** resemble basal epidermal cells but extend into the dermis and form clusters with a palisade arrangement of peripheral cells.

**(Choice F)** **Seborrheic keratosis** forms a hyperpigmented lesion with well-circumscribed borders, a dull surface, and a "stuck-on" appearance. On microscopic examination, the lesions are composed of small cells resembling basal cells, with variable pigmentation, hyperkeratosis, and **keratin-containing cysts**.

### Educational objective:

Compound nevi are benign proliferations of melanocytes that involve both the dermis and epidermis. The



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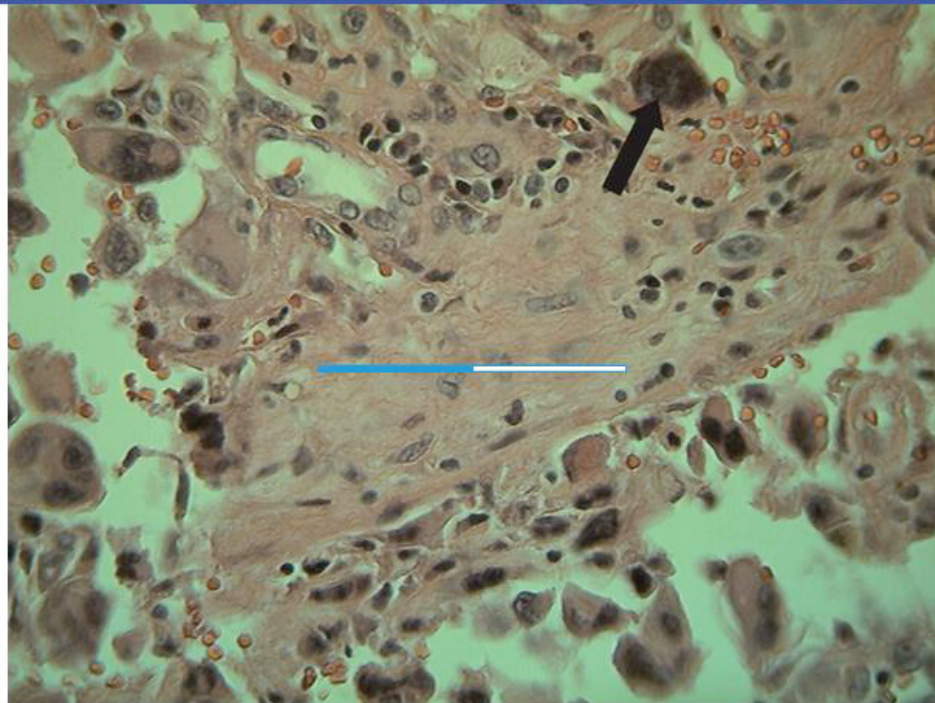


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Exhibit Display



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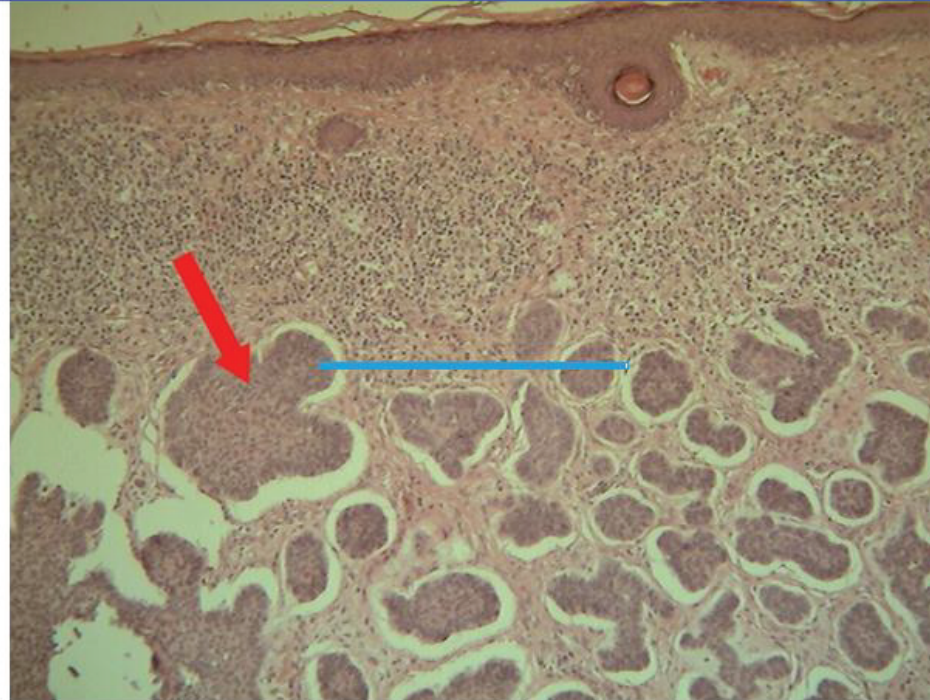
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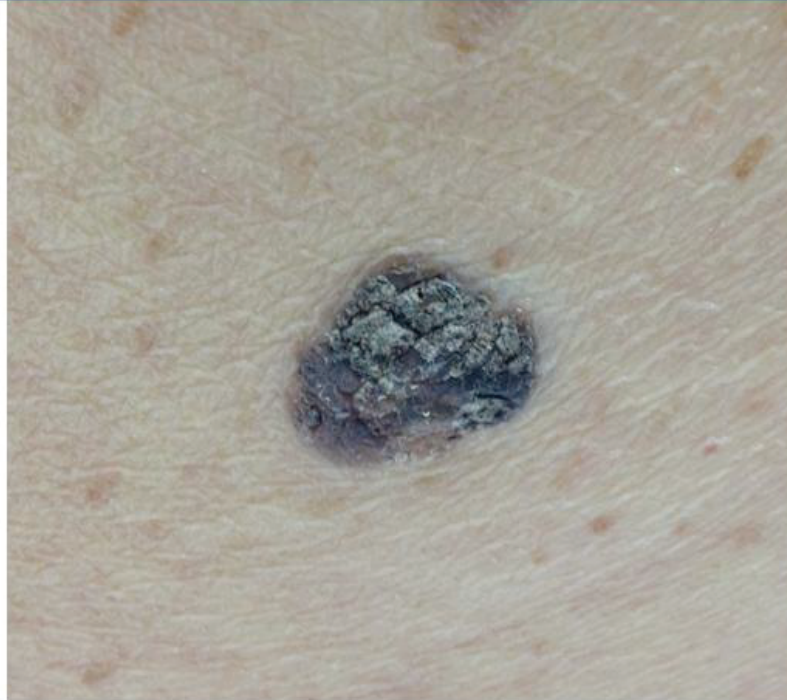
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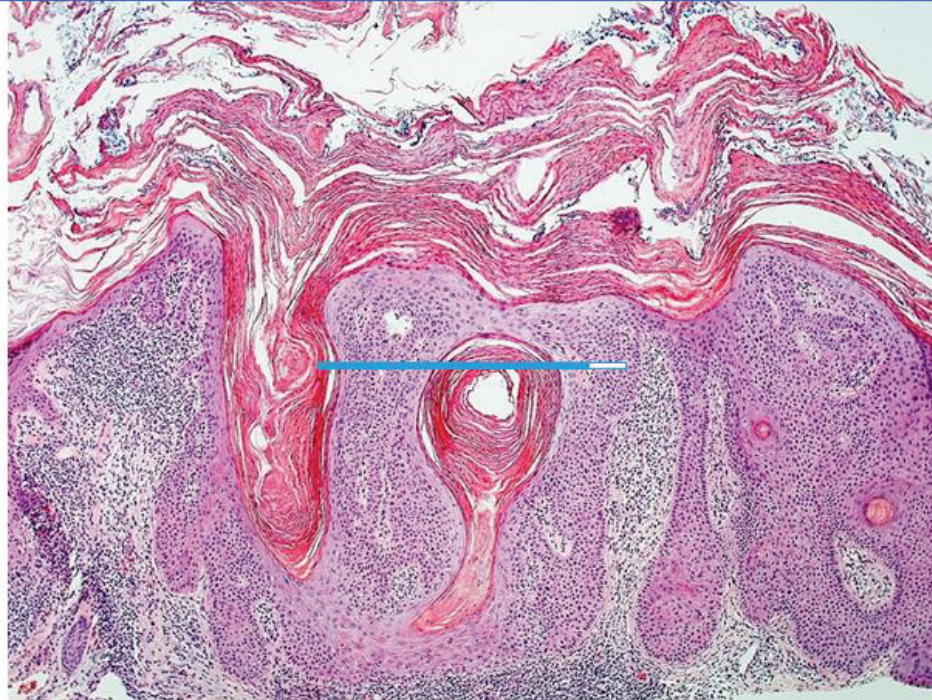
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fuse into a continuous layer at the dermoepidermal border.

**(Choice E)** [Pigmented basal cell carcinoma](#) can present as papules, nodules, or plaques with rolled borders on sun-exposed areas. They can have varying degrees of pigmentation due to functional melanocytes within the lesion. The [tumor cells](#) resemble basal epidermal cells but extend into the dermis and form clusters with a palisade arrangement of peripheral cells.

**(Choice F)** [Seborrheic keratosis](#) forms a hyperpigmented lesion with well-circumscribed borders, a dull surface, and a "stuck-on" appearance. On microscopic examination, the lesions are composed of small cells resembling basal cells, with variable pigmentation, hyperkeratosis, and [keratin-containing cysts](#).

### Educational objective:

Compound nevi are benign proliferations of melanocytes that involve both the dermis and epidermis. The lesions appear as slightly raised papules with uniform pigmentation and symmetrical sharp borders.

### References

- [Optimal management of common acquired melanocytic nevi \(moles\): current perspectives.](#)

Pathology	Dermatology	Melanocytic nevus
Subject	System	Topic



fuse into a continuous layer at the dermoepidermal border.

**(Choice E)** [Pigmented basal cell carcinoma](#) can present as papules, nodules, or plaques with rolled borders on sun-exposed areas. They can have varying degrees of pigmentation due to functional melanocytes within the lesion. The [tumor cells](#) resemble basal epidermal cells but extend into the dermis and form clusters with a palisade arrangement of peripheral cells.

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Pathology	Dermatology	Melanocytic nevus
Subject	System	Topic



A 63-year-old woman comes to the office for a routine preventive examination. She has no significant medical problems and takes no medications. The patient consumes a balanced diet; gets regular exercise; and does not use tobacco, alcohol, or illicit drugs. She is up to date on breast, colon, cervical, and lipid screenings. Her physical examination findings are unremarkable. The patient expresses concern about wrinkles around her eyes that make her "look old." A decrease in which of the following is most likely responsible for this patient's complaint?

- ☐ A. Collagen cross-linking
- ☐ B. Collagen fibril production
- ☐ C. Collagenase synthesis
- ☐ D. Elastin degradation
- ☐ E. Proline hydroxylation

**Submit**



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Settings

A 63-year-old woman comes to the office for a routine preventive examination. She has no significant medical problems and takes no medications. The patient consumes a balanced diet; gets regular exercise; and does not use tobacco, alcohol, or illicit drugs. She is up to date on breast, colon, cervical, and lipid screenings. Her physical examination findings are unremarkable. The patient expresses concern about wrinkles around her eyes that make her "look old." A decrease in which of the following is most likely responsible for this patient's complaint?

- ☐ A. Collagen cross-linking (32%)
- ☒ B. Collagen fibril production (38%)
- ☐ C. Collagenase synthesis (6%)
- ☐ D. Elastin degradation (16%)
- ☐ E. Proline hydroxylation (5%)

**Incorrect**

Correct answer

B



38%

Answered correctly



47 secs

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Multiple environmental factors, especially exposure to ultraviolet (UV) light, contribute to aging of the skin. UVB wavelengths are predominantly absorbed in the upper dermis and contribute to sunburn and increased risk of malignancy. **UVA** wavelengths penetrate deeper into skin and cause **photoaging**. UVA produces reactive oxygen species, which activate multiple inflammatory cell-surface receptors and nuclear transcription factors. This leads to **decreased collagen fibril production**, along with upregulation of matrix metalloproteinases (including collagenases) that subsequently degrade type I and III collagen and elastin (**Choices C and D**).

Photoaging may be visible by age 30-35. Gradual **thinning of the epidermis** is seen, with reduction in subcutaneous fat, blood vessels, hair follicles, sweat ducts, and sebaceous glands. Rete ridges at the dermoepidermal junction become flattened. This loss of subcutaneous tissue causes the skin to become atrophic and more vulnerable to damage. In addition, there is increased **crosslinking** of collagen (**Choice A**), with deposition of collagen breakdown products. The atrophic dermis and increased collagen crosslinking, along with desiccation of the stratum corneum, produce the characteristic wrinkling of photoaged skin.

(**Choice E**) Post-translational hydroxylation of proline residues contributes to the stability of the collagen triple helix. This reaction requires ascorbic acid (vitamin C); deficiency of vitamin C leads to scurvy, which is characterized by impaired production and reduced tensile strength of collagen.



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**(Choice E)** Post-translational hydroxylation of proline residues contributes to the stability of the collagen triple helix. This reaction requires ascorbic acid (vitamin C); deficiency of vitamin C leads to scurvy, which is characterized by impaired production and reduced tensile strength of collagen.

### Educational objective:

Photoaging is a product of excess exposure to ultraviolet A wavelengths and is characterized by epidermal atrophy with flattening of rete ridges. In addition, there is decreased collagen fibril production and increased degradation of collagen and elastin in the dermis.

### References

- [Looking older: fibroblast collapse and therapeutic implications.](#)

Pathophysiology

Dermatology

Aging

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A 25-year-old woman comes to the office due to a 4-week history of a pruritic skin rash. The patient has no chronic medical conditions and takes no medication. Vital signs are normal. On examination, there are pink papules distributed symmetrically over the anterior surfaces of the shins and ankles. Shave biopsy reveals prominent hyperkeratosis along with a thickened granular layer. In addition, there is a bandlike infiltrate of mononuclear cells (predominantly lymphocytes) in the subjacent superficial dermis that involves the overlying epidermis. The rete ridges have a sharpened, sawtooth appearance. The basal layer of the epidermis is degenerated, with scattered colloid bodies. Which of the following is the most likely diagnosis?

- ☐ A. Atopic dermatitis
- ☐ B. Contact dermatitis
- ☐ C. Erythema nodosum
- ☐ D. Lichen planus
- ☐ E. Psoriasis



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chronic medical conditions and takes no medication. Vital signs are normal. On examination, there are pink papules distributed symmetrically over the anterior surfaces of the shins and ankles. Shave biopsy reveals prominent hyperkeratosis along with a thickened granular layer. In addition, there is a bandlike infiltrate of mononuclear cells (predominantly lymphocytes) in the subjacent superficial dermis that involves the overlying epidermis. The rete ridges have a sharpened, sawtooth appearance. The basal layer of the epidermis is degenerated, with scattered colloid bodies. Which of the following is the most likely diagnosis?

- ☐ A. Atopic dermatitis (3%)
- ☐ B. Contact dermatitis (4%)
- ☐ C. Erythema nodosum (9%)
- ☒ D. Lichen planus (61%)
- ☐ E. Psoriasis (20%)

Correct

61%



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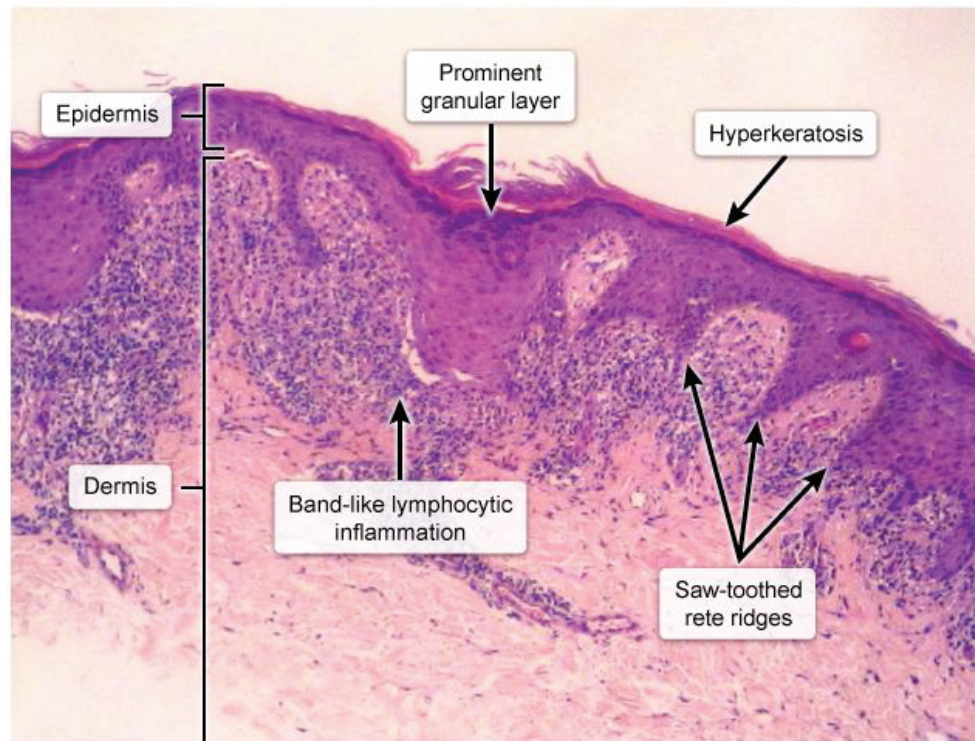
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## Lichen planus



This patient has a pruritic rash consistent with **lichen planus** (LP), an immunologically mediated skin disorder primarily affecting middle-aged adults. The skin lesions typically occur symmetrically on the flexural surfaces of the wrists and ankles but can also involve the nails, oral mucous membranes, and genitalia. The characteristic **skin lesions** are described by the **5 Ps**: **pruritic**, **purple/pink**, **polygonal papules** and **plaques** and can form along lines of minor trauma (**Koebner phenomenon**). Chronic lesions often show white, lacy markings known as **Wickham striae**.

Although the etiology of LP is unknown, it is characterized by a (CD8+) T cell-mediated response to the cells along the junction of the dermis and **epidermis**, resulting in the following characteristic histologic findings:

- Chronic **hyperkeratosis** (thickening of stratum corneum)
- Lymphocytic infiltrates at the dermoepidermal junction (**interface dermatitis**)
- Scattered eosinophilic, **colloid (Civatte) bodies** (apoptotic keratinocytes)
- Hypergranulosis (thickening of stratum granulosum)
- **Sawtooth rete ridges**

**(Choices A and B)** Atopic dermatitis can cause a pruritic rash affecting the extremities, but it usually



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#### Lichen planus



Lacy, scaly, white markings  
(Wickham striae)

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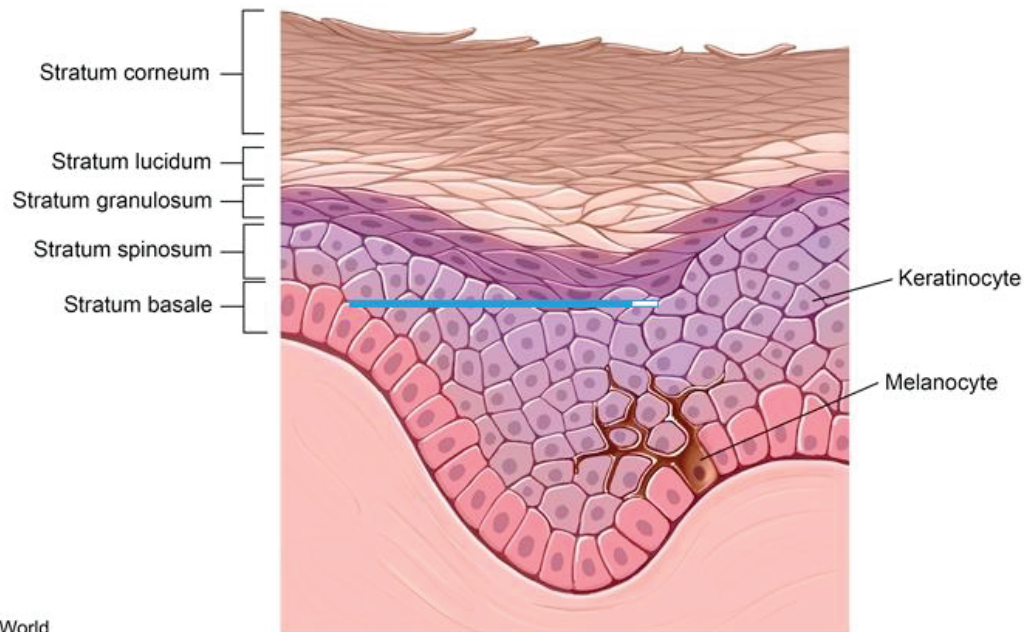
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#### Epidermis of the skin



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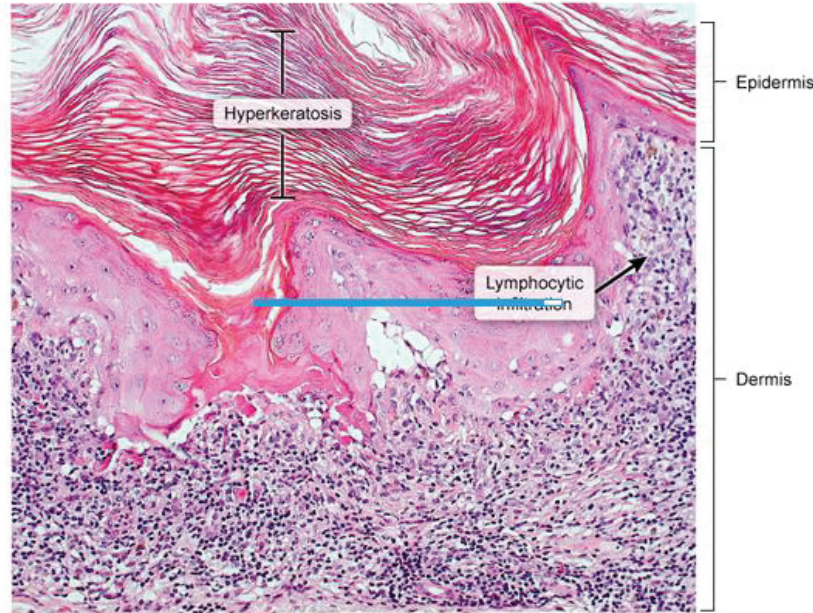
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#### Lichen planus



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**(Choices A and B)** Atopic dermatitis can cause a pruritic rash affecting the extremities, but it usually presents in childhood and most patients have a history of other atopic disorders (eg, allergic rhinitis, asthma). The lesions in contact dermatitis are also pruritic but occur in localized areas corresponding to the specific exposure (eg, waist with nickel belt buckle exposure). Biopsy in these conditions would show spongiosis (epidermal edema) in the acute phase and acanthosis (diffuse epidermal hyperplasia) in chronic disease.

**(Choice C)** Erythema nodosum is a delayed-type hypersensitivity reaction that presents with tender inflammatory nodules in the subcutaneous fat, primarily on the shins. The characteristic histopathologic finding is septal panniculitis in the subcutaneous tissues, with a variable (lymphocytes, neutrophils, macrophages) infiltrate.

**(Choice E)** **Psoriasis** is an immune-mediated inflammatory disease characterized by cytokine-driven keratinocyte hyperproliferation leading to acanthosis with clubbed rete ridges, parakeratosis (retention of nuclei in stratum corneum), and thinned stratum granulosum. It also demonstrates the Koebner phenomenon but usually presents with chronic erythematous plaques with silvery scales on the extensor surfaces of the knees and elbows, scalp, or neck.

### Educational objective:

Lichen planus presents with pruritic, purple/pink, polygonal papules and plaques that can affect the flexural

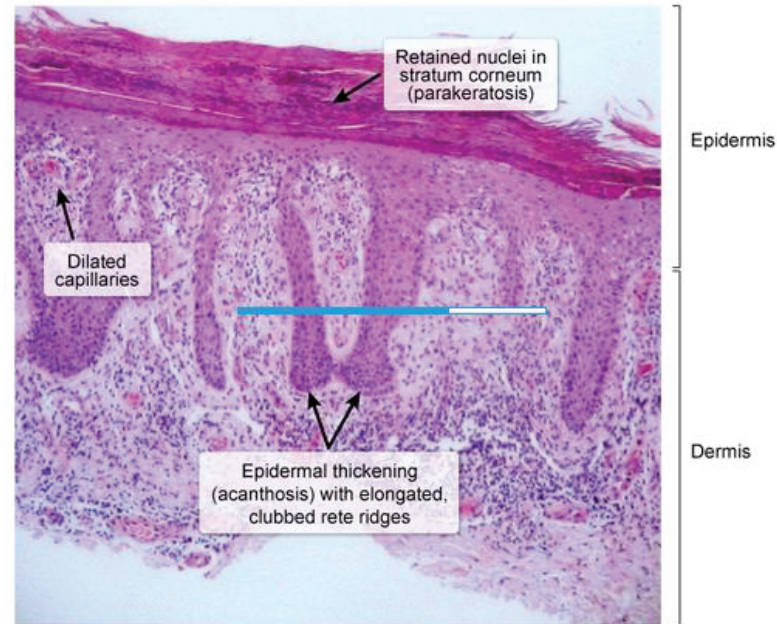


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(Choices A and B) Atopic dermatitis can cause a pruritic rash affecting the extremities, but it usually

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#### Psoriasis



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**(Choice C)** Erythema nodosum is a delayed-type hypersensitivity reaction that presents with tender inflammatory nodules in the subcutaneous fat, primarily on the shins. The characteristic histopathologic finding is septal panniculitis in the subcutaneous tissues, with a variable (lymphocytes, neutrophils, macrophages) infiltrate.

**(Choice E)** **Psoriasis** is an immune-mediated inflammatory disease characterized by cytokine-driven keratinocyte hyperproliferation leading to acanthosis with clubbed rete ridges, parakeratosis (retention of nuclei in stratum corneum), and thinned stratum granulosum. It also demonstrates the Koebner phenomenon but usually presents with chronic erythematous plaques with silvery scales on the extensor surfaces of the knees and elbows, scalp, or neck.

### Educational objective:

Lichen planus presents with pruritic, purple/pink, polygonal papules and plaques that can affect the flexural surfaces of the wrists and ankles, along with the nails, oral mucous membranes, and genitalia. Histologic findings include hyperkeratosis (thickening of stratum corneum), lymphocytic infiltrates at the dermoepidermal junction, hypergranulosis (prominent granular layer), sawtooth rete ridges, and scattered eosinophilic colloid bodies.

Pathology

Dermatology

Lichen planus







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Text Zoom



Settings

A 36-year-old man comes to the office due to a 2-month history of a pruritic rash over the elbows and knees. The patient has been using skin emollients, but the lesions have not improved. He also has a prolonged history of episodic abdominal discomfort, flatulence, and voluminous greasy stools. Cardiopulmonary examination is normal. The abdomen is soft and nontender. Skin examination shows a papulovesicular skin rash in groups with erosion and excoriations. Which of the following is most likely to be seen in this patient?

- ☐ A. Crypt abscesses in colonic mucosa
- ☐ B. IgG-mediated skin disruption
- ☒ C. Increased intestinal intraepithelial lymphocytes
- ☐ D. Increased urinary porphyrins
- ☐ E. Insulin resistance

**Submit**



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Settings

A 36-year-old man comes to the office due to a 2-month history of a pruritic rash over the elbows and knees. The patient has been using skin emollients, but the lesions have not improved. He also has a prolonged history of episodic abdominal discomfort, flatulence, and voluminous greasy stools. Cardiopulmonary examination is normal. The abdomen is soft and nontender. Skin examination shows a papulovesicular skin rash in groups with erosion and excoriations. Which of the following is most likely to be seen in this patient?

- ☐ A. Crypt abscesses in colonic mucosa (19%)
- ☐ B. IgG-mediated skin disruption (9%)
- ☒ C. Increased intestinal intraepithelial lymphocytes (66%)
- ☐ D. Increased urinary porphyrins (2%)
- ☐ E. Insulin resistance (1%)

Correct



66%

Answered correctly



02 mins

Time Spent



11/30/2020

Last Updated

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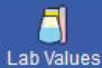


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**Dermatitis herpetiformis (DH)** is characterized by **erythematous pruritic papules, vesicles, and bullae** that appear symmetrically on the extensor surfaces (eg, elbows, knees), upper back, and buttocks.





**Dermatitis herpetiformis (DH)** is characterized by **erythematous pruritic papules, vesicles, and bullae**

that appear symmetrically on the extensor surfaces (eg, elbows, knees), upper back, and buttocks.

Herpetiformis refers to the resemblance of the clustered vesicles to those of herpes simplex. DH is characterized histologically by **microabscesses** containing fibrin and neutrophils at the dermal papillae tips. The overlying basal cells become vacuolated, and coalescing blisters form at the tips of the involved papillae. Immunofluorescent imaging shows **deposition of IgA** at the dermoepidermal junction.

The pathogenesis of DH is associated with that of **celiac disease**. Following absorption of dietary gluten, gliadin is deaminated by tissue transglutaminase in a process involving formation of covalent crosslinks between the two. Because of this, the subsequent immune response against gliadin also targets tissue transglutaminase, leading to the production of IgA and IgG **tissue transglutaminase autoantibodies**. In the skin, these antibodies cross-react with epidermal transglutaminase, and the resulting inflammation leads to the characteristic manifestations of DH.

The majority of patients with DH exhibit the small-bowel histologic findings of celiac disease, which include:

- Small bowel **intraepithelial lymphocytosis**
- Crypt hyperplasia (elongation)
- Progressive **villous atrophy** (height shrinkage)





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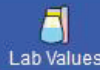
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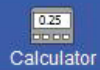
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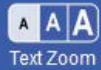
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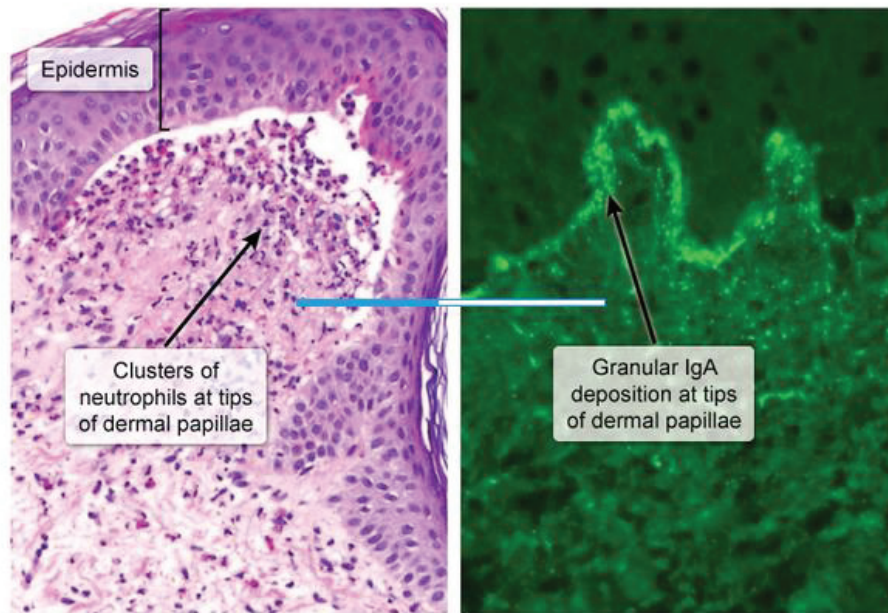
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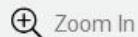
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## Exhibit Display

## Dermatitis herpetiformis



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• Progressive villous atrophy (the donut shrinkage)

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- Small bowel **intraepithelial lymphocytosis**
- Crypt hyperplasia (elongation)
- Progressive **villous atrophy** (height shrinkage)

**(Choice A)** Ulcerative colitis is characterized by mucosal inflammation, crypt abscesses (neutrophils in glandular lumen), and ulcerations. Common dermal associations include **erythema nodosum**, **pyoderma gangrenosum**, and psoriasis. The papulovesicular rash seen in this patient is not consistent with any of these entities.

**(Choice B)** IgG-mediated skin disruption occurs in **pemphigus vulgaris** and **bullous pemphigoid**. These conditions are characterized by large bullae and ulcerations that are not confined to the extensor surfaces. Pemphigus vulgaris may involve the pharynx and esophagus, but neither condition is associated with steatorrhea.

**(Choice D)** Elevated urinary porphyrin levels (ie, uroporphyrin, heptacarboxyl porphyrin) are seen in **porphyria cutanea tarda**. This condition is characterized by skin fragility and blistering lesions in sun-exposed areas. Steatorrhea would be unexpected.

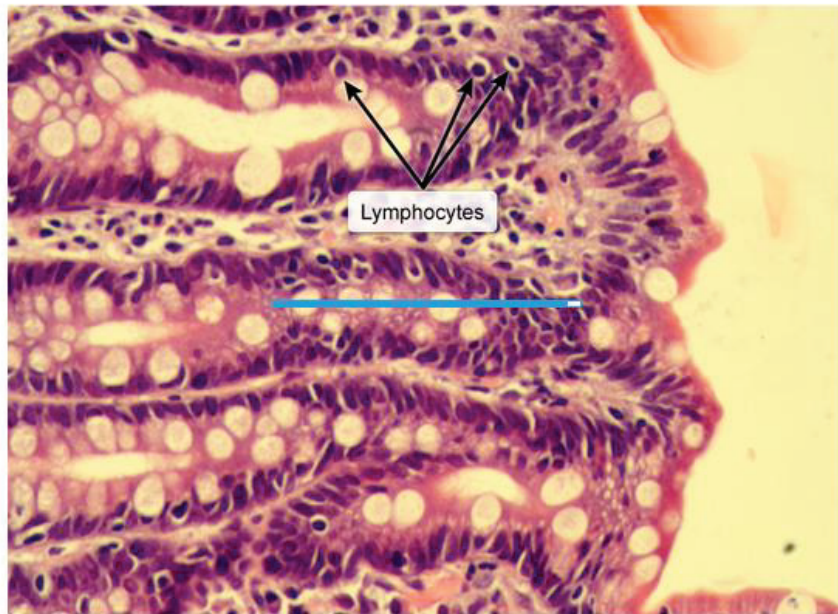
**(Choice E)** Insulin resistance occurs in type 2 diabetes mellitus, which can be associated with **acanthosis nigricans** and **necrobiosis lipoidica diabetorum**. Although celiac disease and DH are associated with





Exhibit Display

Celiac sprue



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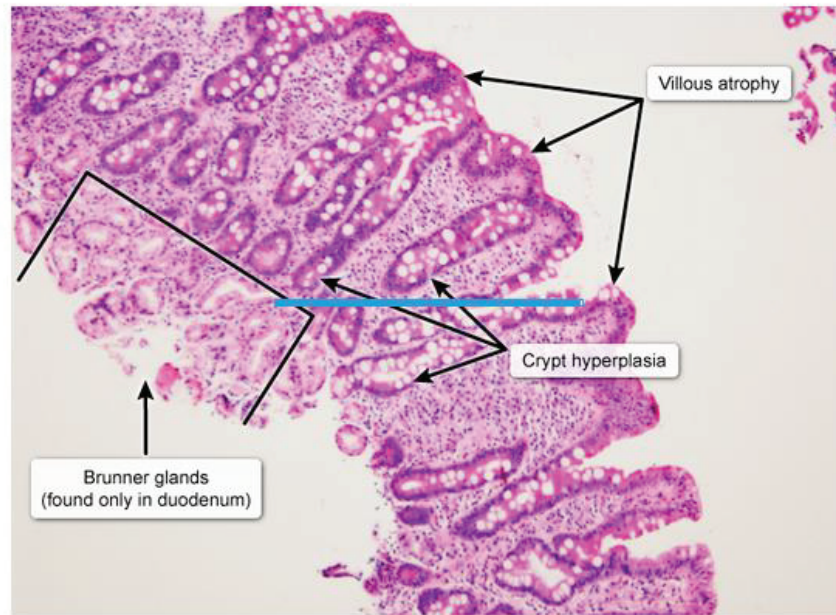
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### Exhibit Display

#### Celiac disease



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Settings

Pemphigus vulgaris may involve the pharynx and esophagus, but neither condition is associated with steatorrhea.

**(Choice D)** Elevated urinary porphyrin levels (ie, uroporphyrin, heptacarboxyl porphyrin) are seen in [porphyria cutanea tarda](#). This condition is characterized by skin fragility and blistering lesions in sun-exposed areas. Steatorrhea would be unexpected.

**(Choice E)** Insulin resistance occurs in type 2 diabetes mellitus, which can be associated with [acanthosis nigricans](#) and [necrobiosis lipoidica diabetorum](#). Although celiac disease and DH are associated with other autoimmune disorders, including type 1 diabetes, there is no association with type 2 diabetes.

### Educational objective:

Dermatitis herpetiformis is characterized by erythematous pruritic papules, vesicles, and bullae that appear symmetrically on extensor surfaces. It is strongly associated with celiac disease, a disorder characterized histologically by small intestinal intraepithelial lymphocytosis, crypt hyperplasia, and villous atrophy.

Pathology

Dermatology

Dermatitis herpetiformis

Subject

System

Topic

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Pemphigus vulgaris may involve the pharynx and esophagus, but neither condition is associated with

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Pemphigus vulgaris may involve the pharynx and esophagus but neither condition is associated with

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Settings

A 34-year-old female presents with a small bluish lesion under the nail of her right index finger. The lesion is extremely tender to touch. If the lesion is a tumor, its cells of origin are most likely to have which of the following functions:

- ☐ A. Proprioception
- ☐ B. Light touch
- ☐ C. Thermoregulation
- ☐ D. Lymphatic drainage
- ☐ E. Antigen processing
- ☐ F. Nail growth

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Settings

A 34-year-old female presents with a small **bluish** lesion under the **nail** of her right index finger. The lesion is extremely tender to touch. If the lesion is a tumor, its cells of origin are most likely to have which of the following functions:

- ☐ A. Proprioception (9%)
- ☐ B. Light touch (24%)
- ☒ C. Thermoregulation (35%)
- ☐ D. Lymphatic drainage (9%)
- ☐ E. Antigen processing (9%)
- ☐ F. Nail growth (11%)

Correct

 35%  
Answered correctly 23 secs  
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Settings

A bluish neoplasm occurring underneath the nail bed may be either a glomus tumor (glomangioma) or a subungual melanoma. Both are rare diagnoses. Melanomas are composed of melanocytes, which have the function of pigmentation. Because 'pigmentation' is not among the answer choices, glomus tumor is the most likely diagnosis.

A glomangioma is a tumor of the modified smooth muscle cells of a glomus body. Glomus bodies are numerous small, encapsulated neurovascular organs found in the dermis of the nail bed, the pads of the fingers and toes, and the ears. Each glomus body is composed of an afferent arteriole connected to a richly innervated, muscular arteriovenous anastomosis, which is then connected to an efferent vein. Modified smooth muscle cells are arranged in layers around these vascular channels. The role of the glomus body is to shunt blood away from the skin surface in cold temperatures in order to prevent heat loss, and to direct blood flow to the skin surface in hot environments to facilitate the dissipation of heat.

**(Choice A)** Extremity receptors responsible for proprioception include muscle spindles, Golgi tendon organs, Pacinian corpuscles, and cutaneous touch receptors (including Meissner's corpuscles, Merkel's disks, and free nerve endings). A tumor of any component of these structures (e.g. neurons, connective tissue cells) would not have a bluish coloration.



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Settings

**(Choice B)** Light touch is mediated by cutaneous mechanoreceptors, which may be encapsulated or free nerve endings. A tumor of these structures would not have a blue hue.

**(Choice D)** A lymphangioma is a tumor of the cells involved in lymphatic drainage. These benign lymphatic neoplasms are analogous to vascular hemangiomas. Lymphangiomas tend to occur subepidermally, in the head, neck, and axilla. They consist of networks of endothelium-lined lymph spaces. Because they do not contain pigmented cells or red blood cells, lymphangiomas would be unlikely to have a bluish appearance.

**(Choice E)** A tumor of antigen-processing cells would be either a histiocytosis or a lymphoma. When there is cutaneous involvement in Langerhans cell histiocytosis, patients present with erythematous papules, nodules, and/or scaling plaques. B-cell lymphomas very rarely involve the skin.

**(Choice F)** The basal epidermal cells of the nail matrix are responsible for nail growth. Tumors originating from the epidermis include squamous cell carcinomas (SCC) and basal cell carcinomas (BCC). SCC does not involve pigmented cells. Although BCC may involve pigmented cells, the majority of these lesions (85%) appear on the head and neck; BCC rarely affects the dorsum of the hands.

### Educational Objective:

A benign glomus tumor (glomangioma) can produce a very tender, small (a few millimeters in diameter)



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Settings

lymphatic neoplasms are analogous to vascular hemangiomas. Lymphangiomas tend to occur subepidermally, in the head, neck, and axilla. They consist of networks of endothelium-lined lymph spaces. Because they do not contain pigmented cells or red blood cells, lymphangiomas would be unlikely to have a bluish appearance.

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**(Choice F)** The basal epidermal cells of the nail matrix are responsible for nail growth. Tumors originating from the epidermis include squamous cell carcinomas (SCC) and basal cell carcinomas (BCC). SCC does not involve pigmented cells. Although BCC may involve pigmented cells, the majority of these lesions (85%) appear on the head and neck; BCC rarely affects the dorsum of the hands.

### Educational Objective:

A benign glomus tumor (glomangioma) can produce a very tender, small (a few millimeters in diameter), red-blue lesion under the nail bed. This type of tumor originates from the modified smooth muscle cells that control the thermoregulatory functions of dermal glomus bodies.

Pathology

Dermatology

Glomus tumor

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Settings

A 32-year-old woman comes to the office due to worry that she will go bald. Her father had a receding hairline with apical baldness beginning at age 20 and was completely bald by age 35. The patient's paternal grandmother and multiple other relatives on her paternal side also had early-onset baldness, but her father's siblings and the maternal side of her family have had no problems with unusual hair loss. Physical examination shows mild thinning of hair at the temporal areas, with an otherwise normal hairline, thickness, and coloration. There is no excess hair growth on her face or trunk, and she has a normal female pattern of pubic hair growth. Palpation of the thyroid is normal. Which of the following is the most likely inheritance pattern of the hair loss in this patient's family?

- ☐ A. Autosomal dominant
- ☐ B. Autosomal recessive
- ☐ C. Mitochondrial
- ☒ D. Polygenic
- ☐ E. Sporadic



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hairline with apical baldness beginning at age 20 and was completely bald by age 35. The patient's paternal grandmother and multiple other relatives on her paternal side also had early-onset baldness, but her father's siblings and the maternal side of her family have had no problems with unusual hair loss. Physical examination shows mild thinning of hair at the temporal areas, with an otherwise normal hairline, thickness, and coloration. There is no excess hair growth on her face or trunk, and she has a normal female pattern of pubic hair growth. Palpation of the thyroid is normal. Which of the following is the most likely inheritance pattern of the hair loss in this patient's family?

- ☐ A. Autosomal dominant (19%)
- ☐ B. Autosomal recessive (23%)
- ☐ C. Mitochondrial (7%)
- ☒ D. Polygenic (45%)
- ☐ E. Sporadic (4%)

Correct

45%



22 secs



01/08/2021

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Settings

### Common medical conditions with polygenic inheritance

- Androgenetic alopecia
- Epilepsy
- Glaucoma
- Hypertension
- Ischemic heart disease
- Schizophrenia
- Type II diabetes mellitus

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The most common type of hair loss in males and females is **androgenetic alopecia** (male pattern baldness). As the name implies, the hair loss is driven by both hormonal (eg, circulating androgens) and genetic factors. The hair loss occurs primarily at the temporal areas and vertex and progresses through life. The pattern and severity vary between males and females.

Androgenetic alopecia demonstrates **polygenic inheritance** with variable expressivity. Key sites of genetic influence have been identified on the short arm of chromosome 20, and also on the X and possibly Y chromosomes. Therefore, some of the genetic factors may be transmitted with X-linked recessive



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Androgenetic alopecia demonstrates **polygenic inheritance** with variable expressivity. Key sites of genetic influence have been identified on the short arm of chromosome 20, and also on the X and possibly Y chromosomes. Therefore, some of the genetic factors may be transmitted with X-linked recessive inheritance (eg, gene variations in the androgen receptor), whereas others will show autosomal dominant inheritance (**Choice A**).

(**Choice B**) Autosomal recessive inheritance classically shows disease development in 25% of offspring from 2 asymptomatic carrier parents. In most cases, conditions with autosomal recessive inheritance will not be seen in consecutive generations.

(**Choice C**) Conditions passed through mitochondrial inheritance are transmitted only by the mother, and all of her offspring are affected. Conditions transmitted by mitochondrial inheritance include a number of uncommon neuromuscular disorders.

(**Choice E**) By definition, sporadic cases do not follow an inheritance pattern. Sporadic cases occur haphazardly among unrelated members of a population over time. For example, there may be a spontaneous gene mutation that causes a sporadic disorder in an individual with no family history of the disease.

**Educational objective:**

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(Choice D) Autosomal recessive inheritance classically shows disease development in 25 % of offspring from 2 asymptomatic carrier parents. In most cases, conditions with autosomal recessive inheritance will not be seen in consecutive generations.

(Choice C) Conditions passed through mitochondrial inheritance are transmitted only by the mother, and all of her offspring are affected. Conditions transmitted by mitochondrial inheritance include a number of uncommon neuromuscular disorders.

(Choice E) By definition, sporadic cases do not follow an inheritance pattern. Sporadic cases occur haphazardly among unrelated members of a population over time. For example, there may be a spontaneous gene mutation that causes a sporadic disorder in an individual with no family history of the disease.

### Educational objective:

Androgenetic alopecia is the most common cause of hair loss in both males and females. The pattern and severity of the baldness depend on both hormonal (circulating androgens) and genetic factors and vary between males and females. The condition is polygenic with variable expressivity.

### References

- Genetic variation in the human androgen receptor gene is the major determinant of common early-onset androgenetic alopecia





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Settings

A 3-year-old girl is brought to the office due to 2 days of fever and rash. Her mother says the patient has also been refusing to eat or drink. She has no prior medical conditions and is up to date with recommended vaccinations. None of the family members have had recent febrile illness, but the patient recently started attending day care. Temperature is 38.3 C (101 F). Physical examination shows multiple small vesicles and ulcers with an erythematous base on the buccal mucosa and tongue. There are similar vesicular lesions on the distal extremities. Which of the following is the most likely underlying cause of this patient's rash?

- ☐ A. Autoantibody-mediated acantholysis
- ☐ B. Disseminated enteroviral infection
- ☐ C. Idiosyncratic hypersensitivity reaction
- ☐ D. Immune response to a bacterial toxin
- ☐ E. Medium-sized arterial inflammation

**Submit**

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A 3-year-old girl is brought to the office due to 2 days of fever and rash. Her mother says the patient has also been refusing to eat or drink. She has no prior medical conditions and is up to date with recommended vaccinations. None of the family members have had recent febrile illness, but the patient recently started attending day care. Temperature is 38.3 C (101 F). Physical examination shows multiple small vesicles and ulcers with an erythematous base on the buccal mucosa and tongue. There are similar vesicular lesions on the distal extremities. Which of the following is the most likely underlying cause of this patient's rash?

- ☐ A. Autoantibody-mediated acantholysis (6%)
- ☒ B. Disseminated enteroviral infection (70%)
- ☐ C. Idiosyncratic hypersensitivity reaction (4%)
- ☐ D. Immune response to a bacterial toxin (10%)
- ☐ E. Medium-sized arterial inflammation (7%)



Enterovirus	
<b>Epidemiology</b>	<ul style="list-style-type: none"><li>• Infants &amp; young children</li><li>• Summer season</li><li>• Fecal-oral transmission</li></ul>
<b>Clinical features</b>	<ul style="list-style-type: none"><li>• Herpangina (oral ulcerations)</li><li>• Hand-foot-and-mouth disease (oral &amp; extremity ulcerations)</li><li>• Aseptic meningitis</li><li>• Myocarditis</li></ul>

This patient's vesicular rash on the buccal mucosa, tongue, and distal extremities likely indicates **hand-foot-and-mouth disease** (HFMD), a common childhood illness caused by species of **Enterovirus** (eg, Coxsackievirus). Transmission largely occurs via the fecal-oral route, and outbreaks are common in **day cares** and elementary schools.

The virus initially replicates in gastrointestinal lymphatic tissue and subsequently **disseminates** through the



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cares and elementary schools.

The virus initially replicates in gastrointestinal lymphatic tissue and subsequently **disseminates** through the reticuloendothelial system and bloodstream to other organs (eg, heart, liver, brain, skin). Patients generally develop low-grade fever and the following mucocutaneous findings:

- **Oral enanthem** – painful, erythematous vesicles and **ulcers** on the tongue and buccal mucosa, which may lead to refusal to eat or drink
- **Skin exanthem** – maculopapular or **vesicular lesions** on the hands, feet, and extremities

Most cases can be managed with supportive care and resolve spontaneously within a week. However, viral shedding in the stool continues for >6 weeks, which can propagate transmission.

**(Choice A)** Pemphigus vulgaris is characterized by autoantibody-mediated acantholysis, which leads to the formation of painful mucous membrane and cutaneous erosions. Vesicles on an *erythematous base* would be atypical; in addition, the palms and soles are generally spared and HFMD is far more common in children.

**(Choice C)** Stevens-Johnson syndrome is a hypersensitivity reaction that is typically triggered by medication (eg, allopurinol) or infection (eg, *Mycoplasma*). It is characterized by necrosis and **detachment**



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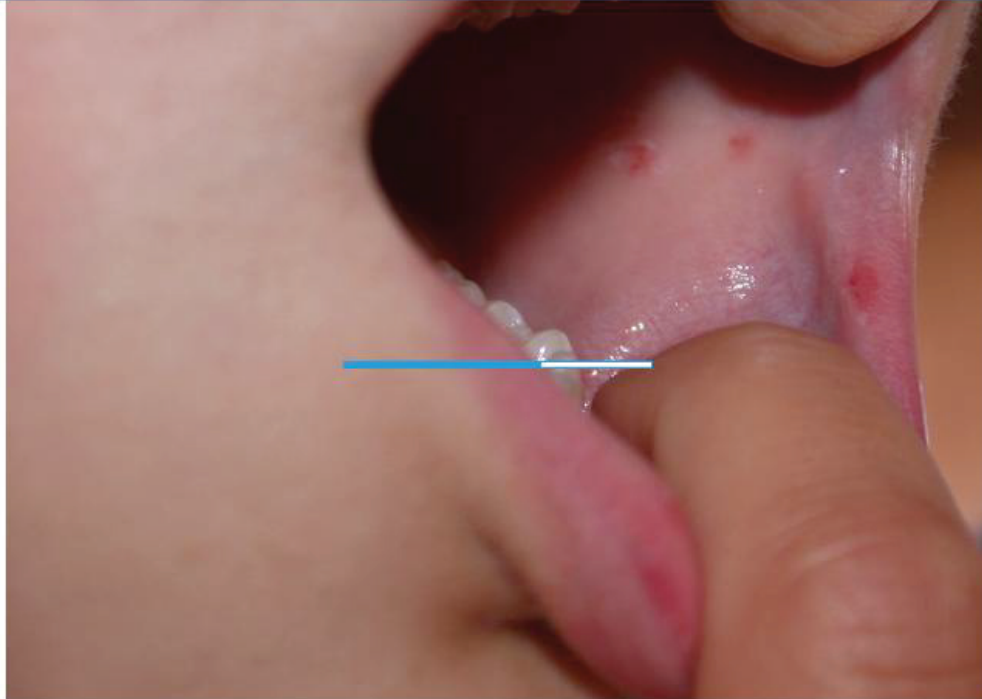



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


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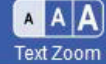
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**(Choice C)** Stevens-Johnson syndrome is a hypersensitivity reaction that is typically triggered by medication (eg, allopurinol) or infection (eg, *Mycoplasma*). It is characterized by necrosis and detachment of the epidermis, leading to high fever; hemorrhagic oral erosions; and coalescing, erythematous skin macules/bullae with purpuric centers.

**(Choice D)** Scarlet fever is a delayed-type immune response to a pyrogenic exotoxin produced by *Streptococcus pyogenes*. Patients usually have a history of streptococcal infection (eg, pharyngitis, cellulitis) and then develop a diffuse, erythematous, papular rash that has a "sandpaper" quality. Vesicles are not typically seen, and the oral cavity is not usually involved.

**(Choice E)** Kawasaki disease is an inflammatory childhood vasculitis that primarily affects medium-sized blood vessels. Patients generally have high fever, mucositis (eg, red lips, strawberry tongue), and a macular or targetoid rash. The presence of vesicles and ulcers makes this diagnosis unlikely.

**Educational objective:**

Hand-foot-and-mouth disease is a common childhood illness characterized by painful, vesicular mouth lesions; ulcers on the extremities; and low-grade fever. It is caused by the ingestion and subsequent dissemination of an enterovirus (eg, Coxsackievirus).



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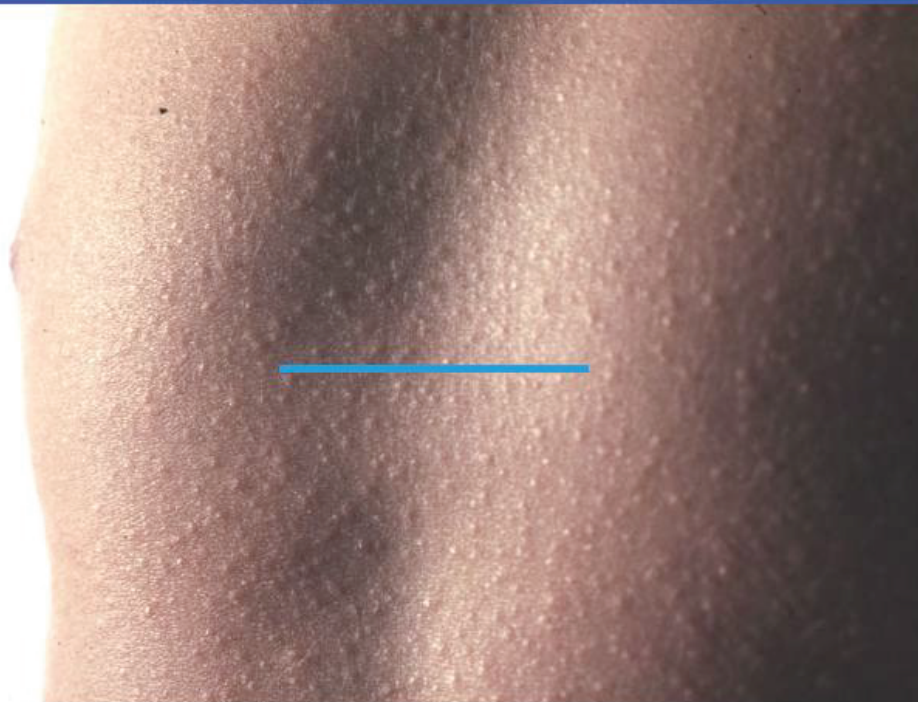
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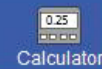
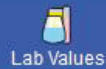
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A 64-year-old man comes to the office with a 4-day history of severe left-sided chest discomfort. The pain is constant and has a burning quality. Over the last day, the patient has developed a rash in the area of discomfort. He has not had similar symptoms before. Past medical history is unremarkable. The patient is afebrile and vital signs are normal. Physical examination shows a vesicular rash at the 5th left intercostal space. Which of the following pathologic findings is most likely to be found in the affected area?

- ☐ A. Acantholysis and intercellular IgG deposits
- ☐ B. Eosinophilic cytoplasmic inclusions
- ☐ C. Koilocytosis of the superficial epidermal layers
- ☐ D. Microabscesses at the tips of dermal papillae
- ☐ E. Multinucleated cells with intranuclear inclusions

Submit





A 64-year-old man comes to the office with a 4-day history of severe left-sided chest **discomfort**. The pain is constant and has a **burning** quality. Over the last day, the patient has developed a rash in the area of discomfort. He has not had similar symptoms before. Past medical history is unremarkable. The patient is afebrile and vital signs are normal. Physical examination shows a vesicular rash at the 5th left intercostal space. Which of the following pathologic findings is most likely to be found in the affected area?

- ☐ A. Acantholysis and intercellular IgG deposits (4%)
- ☐ B. Eosinophilic cytoplasmic inclusions (8%)
- ☐ C. Koilocytosis of the superficial epidermal layers (3%)
- ☐ D. Microabscesses at the tips of dermal papillae (4%)
- ☒ E. Multinucleated cells with intranuclear inclusions (78%)

Correct



78%  
Answered correctly



01 min, 14 secs  
Time Spent



02/26/2021  
Last Updated







**Varicella zoster virus** (VZV) is an enveloped, double-stranded DNA virus transmitted via respiratory droplets or direct contact. Initial infection typically occurs in childhood and causes varicella (chicken pox), which is characterized by fever and a self-limited, diffuse vesicular **rash**. VZV then travels via sensory fibers to the **dorsal root ganglia** (or trigeminal ganglia), where it remains dormant for years. Weakening of cellular immunity leads to reactivation of the virus, which manifests as herpes zoster (**shingles**). Shingles is characterized by unilateral burning pain and a papular or **vesicular rash** in a dermatomal distribution. The lesions coalesce, rupture, crust over, and heal within a few weeks although the discomfort may linger for several weeks.

Light microscopy of a sample from a vesicle base reveals **intranuclear inclusions** in keratinocytes and **multinucleated giant cells** (positive Tzanck smear). Skin biopsy would show acantholysis (loss of intercellular connections) of keratinocytes and intraepidermal vesicles.

**(Choice A)** Acantholysis forming suprabasal blisters is characteristic of **pemphigus vulgaris** (PV). Immunofluorescence reveals deposition of IgG-containing deposits in a reticular pattern around keratinocytes. The immune target in PV is the desmosome protein desmoglein 3.

**(Choice B)** Infection by molluscum contagiosum, a poxvirus, causes eosinophilic **cytoplasmic inclusions**



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keratinocytes. The immune target in PV is the desmosome protein desmoglein 3.

**(Choice B)** Infection by molluscum contagiosum, a poxvirus, causes eosinophilic **cytoplasmic inclusions** (molluscum bodies) in infected cells and dome-shaped, umbilicated **papules** on examination.

**(Choice C)** Human papillomavirus (HPV) infection of the skin presents with **warts** (verruca vulgaris) or squamous cell carcinoma of the penis or vulva, depending on the serotype. Light microscopy reveals cytoplasmic vacuoles in keratinocytes (koilocytosis) and hyperplasia of the epidermis.

**(Choice D)** **Dermatitis herpetiformis** presents with pruritic, grouped vesicles on the extensor surfaces. **Light microscopy** reveals accumulations of neutrophils on the tips of dermal papillae (microabscesses).

### Educational objective:

Herpes zoster (shingles) develops due to reactivation of varicella zoster virus in the dorsal root ganglia (sensory neurons). It presents with a painful vesicular rash in a dermatomal distribution. Intranuclear inclusions in keratinocytes and multinucleated giant cells are seen on light microscopy.

Pathology

Dermatology

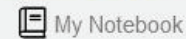
Herpes zoster

Subject


System


Topic








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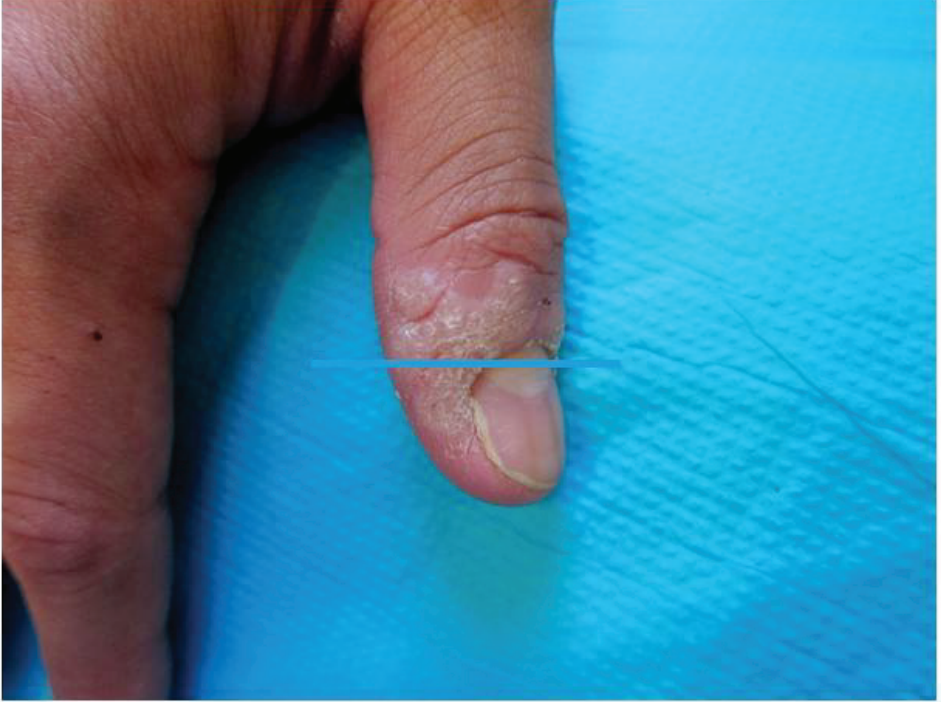
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
A clinical photograph showing a close-up of a person's hand, specifically the index finger. The skin on the finger appears dry, cracked, and there is a small, raised, reddish lesion near the base of the nail. The background is a blue, textured surface.


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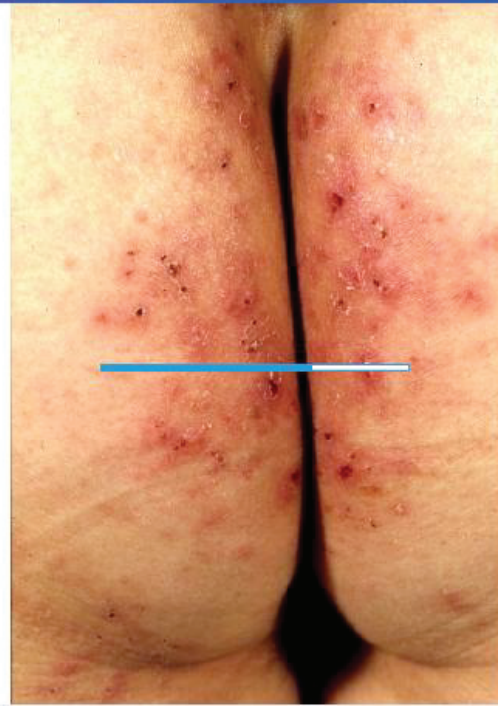


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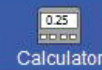
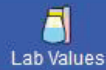


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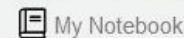
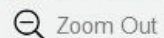
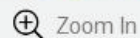


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A 6-month-old boy is brought to the emergency department due to poor feeding, irritability, and rash. He was well-appearing until 2 days ago, when he developed little interest in drinking and a progressive rash. Physical examination reveals diffuse erythema and desquamation that is most prominent at the neck, axillae, inguinal folds, and perioral region. The perioral area also has crusting and the lips are dry and cracked, but the mucosal membranes are normal. The epidermis easily comes off with gentle pressure at the erythematous areas. Which of the following is the most likely cause of this patient's symptoms?

- ☐ A. Autoantibody binding to epithelial cell surface
- ☒ B. Cell-mediated hypersensitivity
- ☐ C. Endotoxin-mediated inflammatory response
- ☐ D. Exotoxin-mediated skin damage
- ☐ E. Mast cell degranulation

**Submit**



A 6-month-old boy is brought to the emergency department due to poor feeding, irritability, and rash. He was well-appearing until 2 days ago, when he developed little interest in drinking and a progressive rash. Physical examination reveals diffuse erythema and desquamation that is most prominent at the neck, axillae, inguinal folds, and perioral region. The perioral area also has crusting and the lips are dry and cracked, but the mucosal membranes are normal. The epidermis easily comes off with gentle pressure at the erythematous areas. Which of the following is the most likely cause of this patient's symptoms?

- ☐ A. Autoantibody binding to epithelial cell surface (11%)
- ☐ B. Cell-mediated hypersensitivity (5%)
- ☐ C. Endotoxin-mediated inflammatory response (11%)
- ☒ D. Exotoxin-mediated skin damage (70%)
- ☐ E. Mast cell degranulation (1%)

Correct



70%

Answered correctly



01 min, 57 secs

Time Spent



09/16/2020

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### Staphylococcal scalded skin syndrome

#### Pathogenesis

- *Staphylococcus aureus* exfoliative toxin
- Cleaves desmoglein in desmosomes → separation of keratinocytes

#### Clinical features

- Fever, irritability
- Generalized erythema, blisters
- Epidermal shedding (Nikolsky sign)

This patient's fever and desquamating rash are most consistent with **staphylococcal scalded skin syndrome** (SSSS), an infection caused by strains of exotoxin-producing *Staphylococcus aureus*.

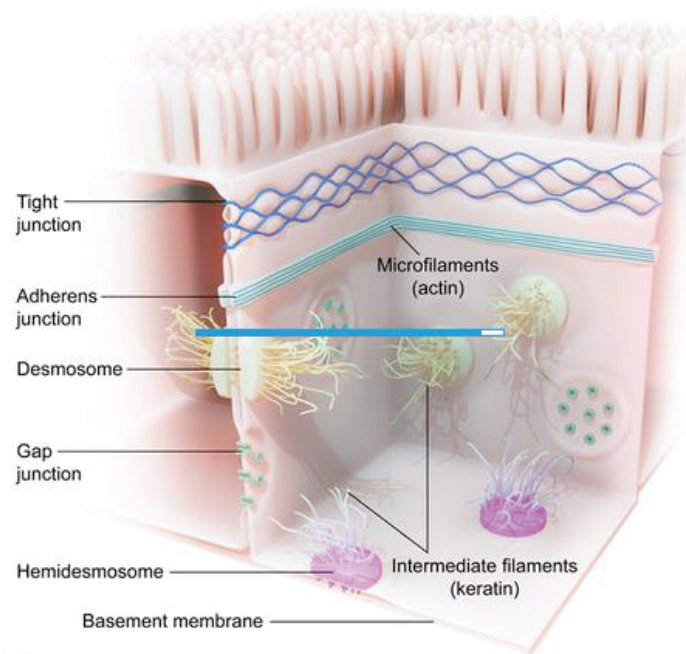
**Exfoliative exotoxins** act as proteases that **cleave desmoglein** in **desmosomes**, which are junctions that adhere epidermal cells together. Skin damage occurs as the exotoxins spread, causing separation of keratinocytes and **superficial epidermal blistering**. Gentle pressure causes detachment and shedding of the outer layer of skin (ie, **Nikolsky sign**). The rash, although diffusely erythematous and **painful** ("scalded"), is most prominent in the **skin folds** (eg, neck, axillae, groin). **Perioral involvement** (eg, erythema, crusting) is common, but the **mucous membranes are spared**.

SSSS is most common in **infants** and **young children**, and skin findings are often preceded or



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(scalded), is most prominent in the **skin folds** (eg, neck, axillae, groin). **Perioral involvement** (eg, erythema, crusting) is common, but the **mucous membranes are spared**.

SSSS is most common in **infants** and **young children**, and skin findings are often preceded or accompanied by fever, irritability, malaise, and poor feeding. Treatment includes antistaphylococcal antibiotics (eg, nafcillin, oxacillin).

**(Choice A)** Pemphigus vulgaris is caused by an autoantibody to desmoglein and results in a positive Nikolsky sign and epidermal erosions, blisters, and bullae. This disorder is uncommon in children, and **mucous membranes** are almost always involved.

**(Choice B)** Cell-mediated (ie, type IV delayed-type) hypersensitivity, in which sensitized  $T_H1$  cells secrete cytokines to attract cytotoxic T cells and NK cells, is responsible for Stevens-Johnson syndrome and toxic epidermal necrolysis. Blistering, bullae, and Nikolsky sign may be seen, but **mucosal involvement** is almost always present. In addition, a preceding trigger (eg, medication, *Mycoplasma pneumoniae* infection) would be expected.

**(Choice C)** Lipopolysaccharides (ie, **endotoxin**) released into the blood by gram-negative bacteria can cause a severe, widespread inflammatory response (septic shock). Purpuric lesions may occur with gram-negative sepsis, but Nikolsky sign would not be present.



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(scalded), is most prominent in the skin folds (eg, neck, axillae, groin). Perioral involvement (eg,

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(scalded), is most prominent in the skin folds (eg, neck, axillae, groin). Perioral involvement (eg,

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be expected.

**(Choice C)** Lipopolysaccharides (ie, *endotoxin*) released into the blood by gram-negative bacteria can cause a severe, widespread inflammatory response (septic shock). Purpuric lesions may occur with gram-negative sepsis, but Nikolsky sign would not be present.

**(Choice E)** Crosslinking of IgE on the cell surface causes mast cell degranulation that is associated with allergic reactions. *Urticaria* (hives) appears as itchy, erythematous, blanching papules, not diffuse erythema or desquamation.

### Educational objective:

Staphylococcal scalded skin syndrome occurs in infants and children due to the production of exfoliative exotoxins by *Staphylococcus aureus*. The toxins cleave desmoglein in desmosomes, leading to widespread epidermal blistering and shedding, especially with gentle pressure (ie, Nikolsky sign). Mucous membranes are spared.

### References

- [Staphylococcal scalded skin syndrome.](#)

Microbiology Dermatology Staphylococcal scalded skin syndrome

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Staphylococcal Scalded Skin Syndrome

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A 25-year-old previously healthy man comes to the office due to penile lesions. The patient first noticed a nontender papule on his penis a month ago, and it has progressively increased in size and number. He reports no fever, dysuria, or penile discharge. The patient is sexually active with multiple partners and uses condoms inconsistently. Physical examination reveals 3 soft, flesh-colored, papillary lesions measuring <1 cm on the dorsum of the penis. There are no enlarged inguinal lymph nodes, and the remainder of the examination is normal. Treatment is started with a topical agent that acts as a toll-like receptor agonist to increase antiviral cytokine production. Which of the following medications was most likely prescribed to this patient?

- ☐ A. Calcipotriene
- ☐ B. Imiquimod
- ☐ C. Pimecrolimus
- ☐ D. Salicylic acid
- ☐ E. Silver nitrate





nontender papule on his penis a month ago, and it has progressively increased in size and number. He reports no fever, dysuria, or penile discharge. The patient is sexually active with multiple partners and uses condoms inconsistently. Physical examination reveals 3 soft, flesh-colored, papillary lesions measuring <1 cm on the dorsum of the penis. There are no enlarged inguinal lymph nodes, and the remainder of the examination is normal. Treatment is started with a topical agent that acts as a toll-like receptor agonist to increase antiviral cytokine production. Which of the following medications was most likely prescribed to this patient?

- ☐ A. Calcipotriene (9%)
- ☒ B. Imiquimod (51%)
- ☐ C. Pimecrolimus (25%)
- ☐ D. Salicylic acid (5%)
- ☐ E. Silver nitrate (7%)

Correct



51%



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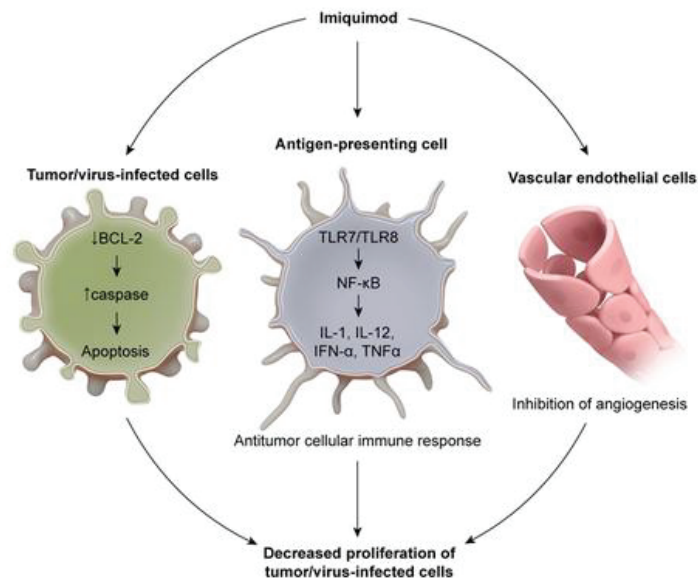
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## Exhibit Display

## Imiquimod mechanism of action



BCL-2 = b-cell lymphoma 2; IL = interleukin; IFN = interferon; TNF = tumor necrosis factor; TLR = toll-like receptor. ©UWorld

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BCL-2 = b-cell lymphoma 2; IL = interleukin; IFN = interferon; TNF = tumor necrosis factor; TLR = toll-like receptor.

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**Imiquimod** is a topical immunomodulatory drug that is used to treat many common dermatologic disorders associated with abnormal cell proliferation, including anogenital warts (ie, human papillomavirus infection), superficial basal cell carcinoma, and actinic keratosis. The antiviral and **antiproliferative** effects of imiquimod are primarily mediated through activation of **toll-like receptor 7**, which upregulates the proinflammatory transcription factor nuclear factor-kappa B (**NF-κB**).

NF-κB increases transcription of proinflammatory genes, activating antigen-presenting cells (eg, Langerhans cells in the skin) and initiating an immune response involving natural killer cells, cytotoxic T cells, and **type 1 helper T cells**. This results in **increased cytokine production** (eg, IL-1, IL-12, interferon-alfa/gamma, tumor necrosis factor-alpha) and enhanced immune-mediated killing of aberrant cells (eg, cancer cells, virus-infected cells).

Other antiproliferative effects of imiquimod include:

- Induction of **apoptosis** of aberrant cells through **caspase activation** via inhibition of BCL-2
- **Inhibition of angiogenesis** by downregulating proangiogenic factors (eg, fibroblast growth factor) and upregulating angiogenesis inhibitors (eg, interferon-gamma, IL-12)



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Settings

**(Choice A)** Calcipotriene is a vitamin D analog (ie, activates the vitamin D receptor, a nuclear transcription factor) used to treat plaque psoriasis. It acts by inhibiting T-cell and keratinocyte proliferation and stimulating keratinocyte differentiation.

**(Choice C)** Pimecrolimus is a calcineurin inhibitor used to treat atopic dermatitis (eczema). It acts by blocking the translocation of NFAT (nuclear factor of activated T cells), resulting in reduced transcription of IL-2.

**(Choice D)** Topical salicylic acid is a keratolytic agent that acts by increasing sloughing of virus-infected epidermal cells. It is widely used to treat common warts but is not recommended for anogenital warts.

**(Choice E)** Silver nitrate is a caustic agent that coagulates cellular proteins to form an eschar. It is used to cauterize wounds to stop bleeding (eg, epistaxis) and to remove excess granulation tissue.

**Educational objective:**

Imiquimod is a widely used topical immunomodulatory agent that stimulates a potent cellular and cytokine-based immune response to aberrant cells (eg, human papillomavirus-infected cells in anogenital warts) by activating toll-like receptors and upregulating NF- $\kappa$ B. Other antiproliferative effects of imiquimod include inhibition of angiogenesis and induction of apoptosis.



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An 18-year-old man comes to the office due to acne. The patient has had mild facial acne for the past 3 years that has responded well to topical agents. Since he started college 2 months ago, the acne has worsened and has spread to his torso and neck. Despite use of the topical agents, it has continued to worsen. The patient plays on the university's baseball team, which requires him to practice outdoors for several hours 3 days a week. He also swims in an indoor pool several hours a week. Since starting college, the patient has adopted a dairy-free, low-glycemic-index diet. Physical examination shows severe, nodulocystic acne on the face, neck, chest, and back. Which of the following most likely caused this patient's worsening acne?

- ☐ A. Dairy-free diet
- ☐ B. Exposure to chlorinated water
- ☐ C. Low-glycemic-index diet
- ☐ D. Methyltestosterone supplementation
- ☐ E. Ultraviolet radiation







years that has responded well to topical agents. Since he started college 2 months ago, the acne has worsened and has spread to his torso and neck. Despite use of the topical agents, it has continued to worsen. The patient plays on the university's baseball team, which requires him to practice outdoors for several hours 3 days a week. He also swims in an indoor pool several hours a week. Since starting college, the patient has adopted a dairy-free, low-glycemic-index diet. Physical examination shows severe, nodulocystic acne on the face, neck, chest, and back. Which of the following most likely caused this patient's worsening acne?

- ☐ A. Dairy-free diet (1%)
- ☐ B. Exposure to chlorinated water (9%)
- ☐ C. Low-glycemic-index diet (2%)
- ☒ D. Methyltestosterone supplementation (76%)
- ☐ E. Ultraviolet radiation (10%)

Correct



76%

Answered correctly



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11/03/2020

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### Acne vulgaris

<b>Clinical features</b>	<ul style="list-style-type: none"> <li>• Comedonal acne: closed or open comedones on forehead, nose &amp; chin</li> <li>• Inflammatory acne: small, erythematous papules &amp; pustules</li> <li>• Nodular acne: large, painful nodules; sinus tracts &amp; scarring</li> </ul>
<b>Pathogenesis</b>	<ul style="list-style-type: none"> <li>• Hyperkeratinization &amp; obstruction of pilosebaceous follicle</li> <li>• Sebaceous gland enlargement &amp; increased sebum production</li> <li>• Metabolism of sebaceous lipids by <i>Cutibacterium acnes</i> &amp; release of inflammatory fatty acids</li> <li>• Follicular inflammation &amp; rupture</li> </ul>
<b>Risk factors</b>	<ul style="list-style-type: none"> <li>• Increased circulating androgens (eg, puberty, polycystic ovary syndrome)</li> <li>• Mechanical trauma/friction (eg, excessive scrubbing, tight clothing)</li> <li>• Comedogenic oil-based skin &amp; hair products</li> </ul>

This college athlete's rapidly worsening acne despite the previously effective use of topical agents raises concern for **androgenic steroid supplementation**. Androgens (eg, dehydroepiandrosterone, testosterone) are produced predominantly by the adrenal glands and gonads; they may also be



This college athlete's rapidly worsening acne despite the previously effective use of topical agents raises concern for **androgenic steroid supplementation**. Androgens (eg, dehydroepiandrosterone, testosterone) are produced predominantly by the adrenal glands and gonads; they may also be supplemented exogenously. They bind to receptors in cytosol, translocate into the nucleus, and alter gene expression. In the skin, this results in increased **sebum production** by sebaceous glands and **follicular epidermal hyperproliferation**, which promote **acne formation**.

The role that androgens play in acne pathogenesis is clearly demonstrated in the **prepubertal** and **pubertal** years, when a rise in adrenal and gonadal androgens coincides with acne formation. Hirsute women with pathologic hyperandrogenic states (eg, **polycystic ovary syndrome**) also frequently have coexisting acne. When acne suddenly becomes severe (eg, nodulocystic acne, **acne fulminans**), androgenic steroid supplementation should be considered as a possible cause, especially in athletes.

**(Choices A and C)** Dairy consumption (particularly skim milk) and a high-glycemic-index diet are associated with acne. Natural hormones in milk and increased levels of insulin-like growth factor may play a role.

**(Choice B)** Chlorine has antibacterial effects against *Cutibacterium acnes*, the bacteria which promotes inflammation in acne. Regular exposure to chlorinated water may improve acne.







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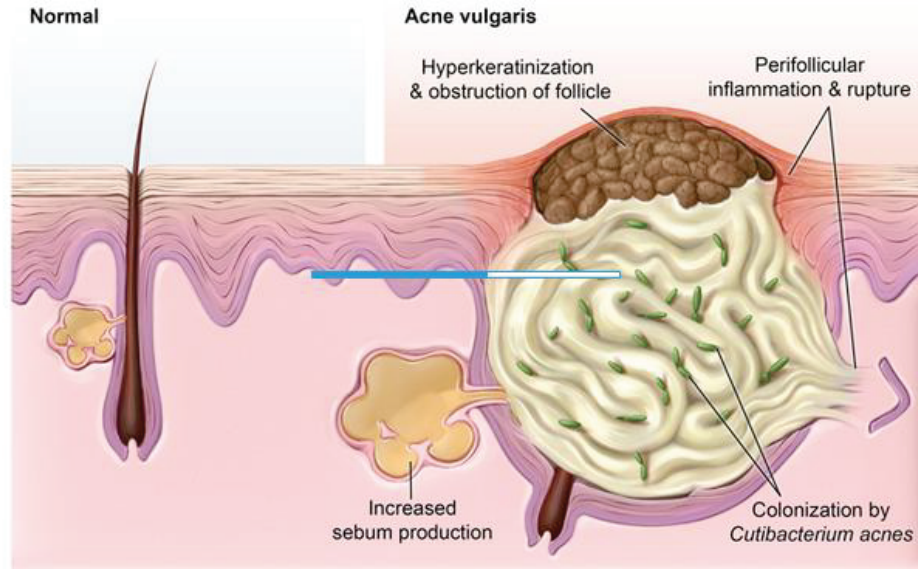
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## Exhibit Display

## Pathogenesis of acne



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androgenic steroid supplementation should be considered as a possible cause, especially in athletes.

**(Choices A and C)** Dairy consumption (particularly skim milk) and a high-glycemic-index diet are associated with acne. Natural hormones in milk and increased levels of insulin-like growth factor may play a role.

**(Choice B)** Chlorine has antibacterial effects against *Cutibacterium acnes*, the bacteria which promotes inflammation in acne. Regular exposure to chlorinated water may improve acne.

**(Choice E)** Ultraviolet radiation can cause sunburn or precipitate photodermatoses, such as the malar rash seen in systemic lupus erythematosus or drug-induced photosensitivity (eg, tetracyclines, sulfonamides). However, ultraviolet radiation would not suddenly cause severe acne.

### Educational objective:

Androgens stimulate follicular epidermal hyperproliferation and excessive sebum production, thereby promoting acne development. Androgenic steroid supplementation is a known cause of acne, especially in competitive athletes.

Pharmacology

Dermatology

Androgenic steroids

Subject

System

Topic







A 64-year-old man comes to the emergency department due to worsening left lower extremity pain, swelling, and redness over the past 3 days. The patient has had no trauma but reports feeling feverish. Medical history is significant for hypertension and obesity. Temperature is 38 C (100.4 F), blood pressure is 130/86 mm Hg, pulse is 92/min, and respirations are 18/min. BMI is 35 kg/m<sup>2</sup>. Physical examination shows diffuse erythema extending up to the left midcalf with indistinct border. There is increased warmth, tenderness, and edema of the left leg. No areas of fluctuation or purulent exudate are present, but the interdigital skin of the feet is macerated and fissured. Laboratory testing shows neutrophilic leukocytosis, and Doppler ultrasonography is negative for deep venous thrombosis. Infection with which of the following organisms is most likely responsible for this patient's current symptoms?

- ☐ A. Beta-hemolytic streptococci
- ☐ B. *Candida albicans*
- ☐ C. *Clostridium perfringens*
- ☐ D. *Mycobacterium marinum*
- ☐ E. *Pseudomonas aeruginosa*



swelling, and redness over the past 3 days. The patient has had no trauma but reports feeling feverish.

Medical history is significant for hypertension and obesity. Temperature is 38 C (100.4 F), blood pressure is 130/86 mm Hg, pulse is 92/min, and respirations are 18/min. BMI is 35 kg/m<sup>2</sup>. Physical examination shows diffuse erythema extending up to the left midcalf with indistinct border. There is increased warmth, tenderness, and edema of the left leg. No areas of fluctuation or purulent exudate are present, but the interdigital skin of the feet is macerated and fissured. Laboratory testing shows neutrophilic leukocytosis, and Doppler ultrasonography is negative for deep venous thrombosis. Infection with which of the following organisms is most likely responsible for this patient's current symptoms?

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- ☐ B. *Candida albicans*
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- ☐ D. *Mycobacterium marinum*
- ☐ E. *Pseudomonas aeruginosa*
- ☐ F. *Staphylococcus epidermidis*

130/86 mm Hg, pulse is 92/min, and respirations are 18/min. BMI is 35 kg/m<sup>2</sup>. Physical examination shows diffuse erythema extending up to the left midcalf with indistinct border. There is increased warmth, tenderness, and edema of the left leg. No areas of fluctuation or purulent exudate are present, but the interdigital skin of the feet is macerated and fissured. Laboratory testing shows neutrophilic leukocytosis, and Doppler ultrasonography is negative for deep venous thrombosis. Infection with which of the following organisms is most likely responsible for this patient's current symptoms?

- ✓ ☐ A. Beta-hemolytic streptococci (55%)
- ☐ B. *Candida albicans* (3%)
- ☐ C. *Clostridium perfringens* (11%)
- ☐ D. *Mycobacterium marinum* (3%)
- ✗ ☒ E. *Pseudomonas aeruginosa* (13%)
- ☐ F. *Staphylococcus epidermidis* (12%)

Incorrect

Correct answer

55%

01 min, 23 secs

11/17/2020

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**Cellulitis** is an acute bacterial infection of the skin and subcutaneous tissues that is marked by a few days of spreading skin erythema, warmth, and tenderness. Many patients also have associated fever, leukocytosis, and localized lymphadenopathy. Most cases are driven by disruptions to the skin barrier due to minor trauma, lymphedema, or dermatophytic infection, which allow a portal of entry for bacteria.

Cases of cellulitis are generally divided as follows:

- **Nonpurulent cellulitis** is characterized by skin warmth, edema, and **erythema** with **no fluctuant nodules**. It is most often caused by **beta-hemolytic streptococci** (groups A, B, C, G, and F); group A streptococcus (*Streptococcus pyogenes*) accounts for the majority of cases.
- **Purulent cellulitis** is characterized by a painful, fluctuant nodule in the dermis or subcutaneous tissue with or without surrounding erythema. The most common cause is *Staphylococcus aureus*; strains that express the virulence factor Panton-Valentine leukocidin are particularly likely to cause skin abscess.

**(Choice B)** *Candida albicans* is a skin commensal that can cause inflammatory, moist, weeping, erythematous lesions in skin folds. It is not a common cause of acute, spreading cellulitis.

**(Choice C)** *Clostridium perfringens* causes gas gangrene after traumatic injury (eg, knife wound, surgery)



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erythematous lesions in skin folds. It is not a common cause of acute, spreading cellulitis.

**(Choice C)** *Clostridium perfringens* causes gas gangrene after traumatic injury (eg, knife wound, surgery) to the skin and soft tissue. It is usually characterized by sudden-onset severe pain, bullous skin lesions, and signs of systemic toxicity/sepsis.

**(Choice D)** *Mycobacterium marinum* skin infection is usually associated with saltwater exposure and is generally characterized by solitary papules that ulcerate and scar.

**(Choice E)** *Pseudomonas aeruginosa* skin infections are most common in those who have had exposure to a hot tub ("hot tub folliculitis") or in patients with diabetes mellitus (eg, diabetic foot infection). It is a much less common cause of cellulitis than beta-hemolytic streptococci.

**(Choice F)** *Staphylococcus epidermis* is a low-virulence skin commensal that rarely causes cellulitis. However, it may occasionally cause bacteremia in patients with intravenous catheters.

### Educational objective:

The most common cause of nonpurulent cellulitis is beta-hemolytic streptococci, particularly group A streptococcus. The most common cause of purulent cellulitis is *Staphylococcus aureus*.

### References





A 55-year-old man is evaluated due to a nonhealing left forearm wound. The patient had an excisional biopsy of a suspicious skin lesion at the site of the wound several weeks ago. He has a history of uncontrolled type 2 diabetes mellitus and hypertension. Vital signs are within normal limits. Physical examination shows a 2.5-cm wound surrounded by erythema on the left forearm. Upregulation of which of the following would most likely improve fibroblast proliferation and reepithelization in this nonhealing wound?

- ☐ A. Bradykinin release from endothelial cells
- ☐ B. Cortisol release from the adrenal cortex
- ☐ C. Glycation cross-links in collagen fibers
- ☐ D. Production of IL-10 by macrophages
- ☐ E. Release of reactive oxygen species from neutrophils

**Submit**



A 55-year-old man is evaluated due to a **nonhealing left** forearm wound. The patient had an excisional biopsy of a suspicious skin lesion at the site of the wound several weeks ago. He has a history of uncontrolled type 2 diabetes mellitus and hypertension. Vital signs are within normal limits. Physical examination shows a 2.5-cm wound surrounded by erythema on the left forearm. Upregulation of which of the following would most likely improve fibroblast proliferation and reepithelization in this nonhealing wound?

- ☐ A. Bradykinin release from endothelial cells (8%)
- ☒ B. Cortisol release from the adrenal cortex (2%)
- ☐ C. Glycation cross-links in collagen fibers (28%)
- ☒ D. Production of IL-10 by macrophages (58%)
- ☐ E. Release of reactive oxygen species from neutrophils (1%)

**Incorrect**

Correct answer



58%

Answered correctly



02 mins, 44 secs

Time Spent



09/15/2020

Last Updated

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This patient with a history of uncontrolled diabetes mellitus has a nonhealing wound with evidence of ongoing inflammation (eg, erythema).

**Wound healing** normally progress through the inflammatory, proliferative, and remodeling phases. In the days after the initial injury, neutrophils and other immune cells are recruited to the wound and produce an **inflammatory response** that helps prevent bacterial overgrowth in the nutrient-rich environment of a healing wound. However, this inflammation also **impairs formation of granulation tissue** that is needed for normal wound healing. As healing progresses, release of growth factors and **anti-inflammatory cytokines** (eg, IL-10) by macrophages and regulatory T cells suppresses the inflammatory response, **facilitating fibroblast proliferation** and reepithelialization of the wound.

In patients with diabetes mellitus, constitutively **elevated blood glucose** increases inflammation by stimulating the release of **proinflammatory cytokines** and reactive oxygen species from neutrophils (**Choice E**). Elevated glucose also leads to a marked **decrease in IL-10** production that contributes to the increased susceptibility for chronic, **nonhealing wounds** and ulcers in patients with uncontrolled diabetes.

(**Choice A**) Bradykinin is a vasoactive inflammatory mediator that is normally produced by endothelial cells, macrophages, and platelets during the inflammatory phase of wound healing. Further upregulation of inflammatory mediators in patients with diabetes would most likely have a negative effect on fibroblast







**(Choice A)** Bradykinin is a vasoactive inflammatory mediator that is normally produced by endothelial cells, macrophages, and platelets during the inflammatory phase of wound healing. Further upregulation of inflammatory mediators in patients with diabetes would most likely have a negative effect on fibroblast proliferation and reepithelialization.

**(Choice B)** Although a baseline level of cortisol production is required for normal wound healing, excess cortisol can impair both the inflammatory and proliferative components of wound healing. Patients with diabetes tend to have elevated cortisol levels; therefore, further cortisol elevation would not improve wound healing.

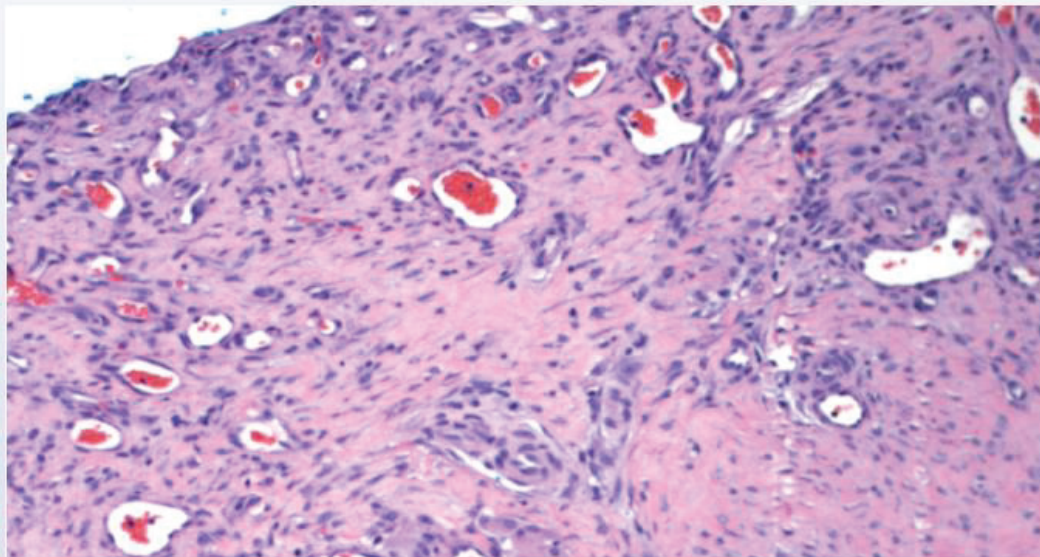
**(Choice C)** Excess glucose inhibits fibroblast migration and results in the nonenzymatic glycation of collagen fibers, which can prevent collagen cross-linking and can impair the structural integrity of a healing wound.

**Educational objective:**

Elevated blood glucose induces the release of reactive oxygen species and proinflammatory cytokines from neutrophils while inhibiting the production of anti-inflammatory cytokines (eg, IL-10) and growth factors needed for fibroblast proliferation and reepithelialization in a healing wound. As a result, patients with uncontrolled diabetes frequently have nonhealing wounds with evidence of ongoing inflammation.



A 72-year-old man is evaluated due to a scaly lesion behind his right ear. A diagnosis of squamous cell carcinoma is confirmed on biopsy, and the patient undergoes excision of the lesion with clear margins. The wound is left to heal by secondary intention. Three weeks later, the patient returns to the office with a 2.5-cm raised, soft, granular lesion at the excision site. Biopsy of a representative lesion is shown in the image below:







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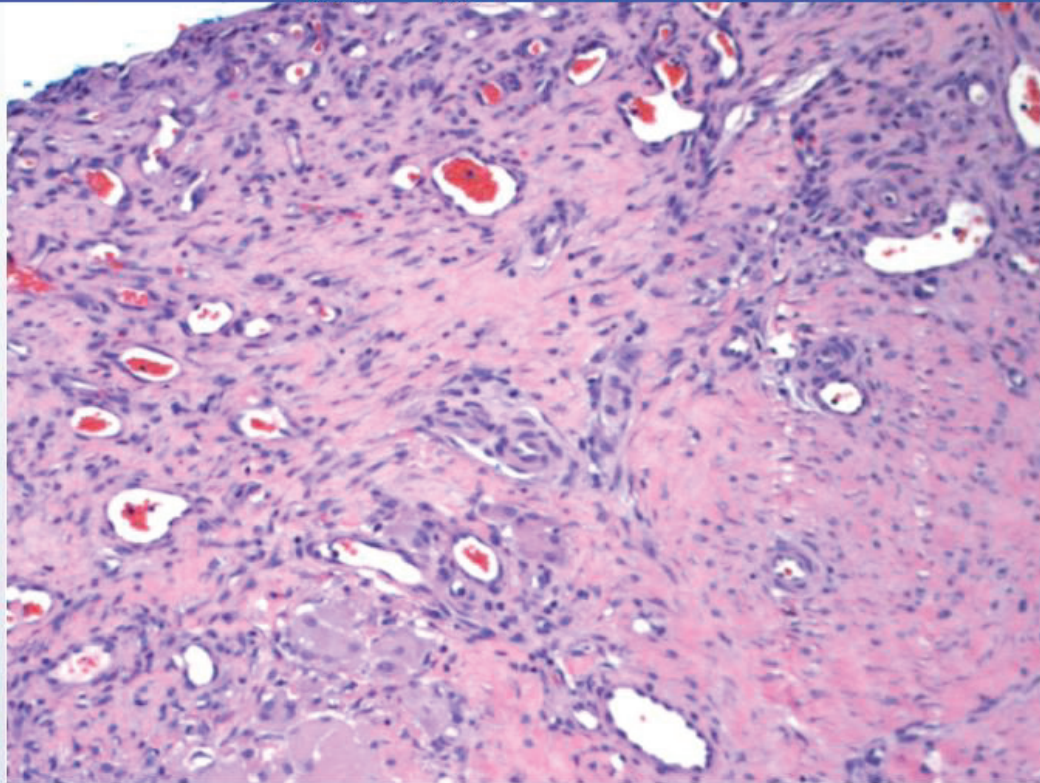
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Which of the following is most likely responsible for this patient's postoperative changes?

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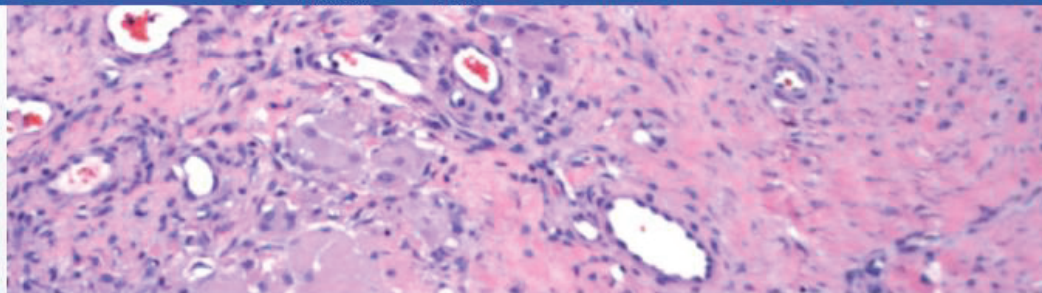
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Which of the following is most likely responsible for this patient's postoperative changes?

- ☐ A. Deposition of immunoglobulin-derived fibrils
- ☐ B. Excess production of type I collagen
- ☐ C. Proliferation of dysplastic keratinocytes
- ☒ D. Recruitment and degranulation of neutrophils
- ☐ E. VEGF-induced tissue proliferation

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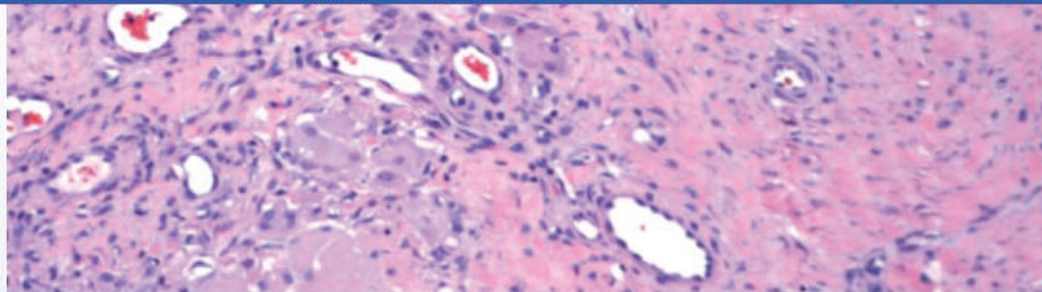
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Which of the following is most likely responsible for this patient's postoperative changes?

- ☐ A. Deposition of immunoglobulin-derived fibrils (1%)
- ☒ B. Excess production of type I collagen (40%)
- ☐ C. Proliferation of dysplastic keratinocytes (4%)
- ☐ D. Recruitment and degranulation of neutrophils (2%)
- ☒ E. VEGF-induced tissue proliferation (51%)

**Incorrect**

Correct answer

51%

Answered correctly



01 min, 53 secs

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Last updated

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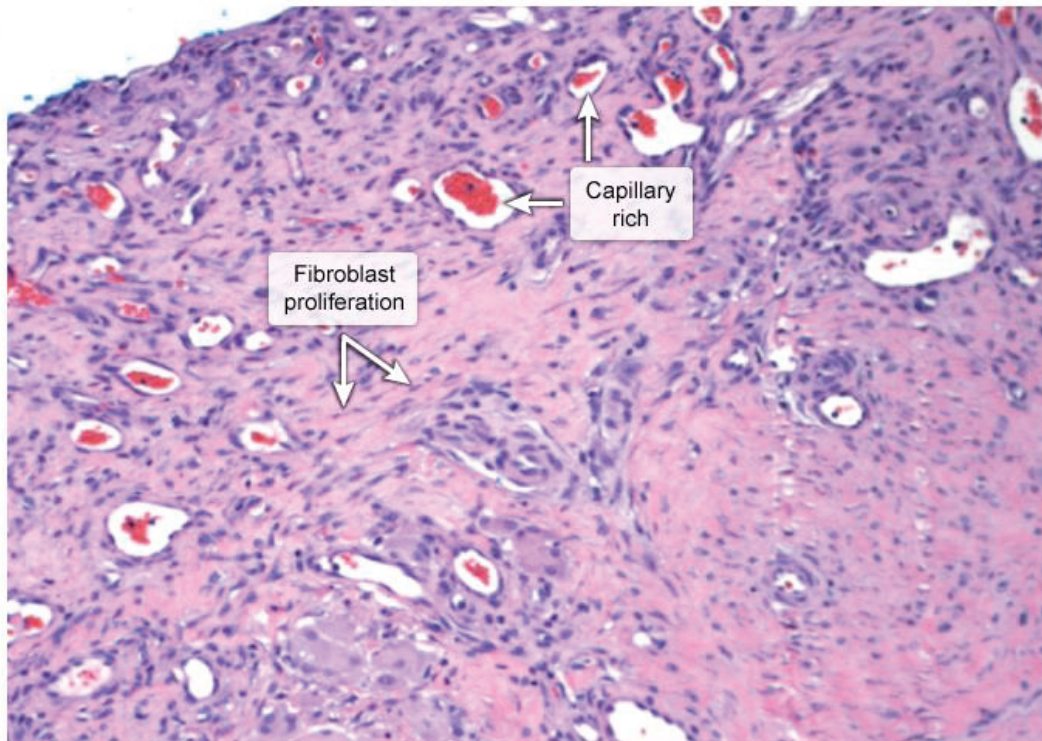


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### Granulation tissue





This patient has a lesion with **abundant capillaries and fibroblasts**, which is characteristic of **granulation tissue**. Raising of the lesion above the surrounding skin (tissue overgrowth) is further consistent with excessive proliferation of granulation tissue (ie, **hypergranulation tissue**) at the site of wound healing.

Granulation tissue is an essential component of the proliferative phase of normal wound healing, providing the nutrients and structure needed for a wound to fill and reepithelialize. Platelets and macrophages in and around a healing wound produce vascular endothelial growth factor (VEGF), which induces the vascular and fibroblast proliferation of granulation tissue.

However, if **VEGF-induced tissue proliferation** continues unchecked, the resulting hypergranulation tissue prevents wound epithelialization and remodeling. These lesions most often occur at the site of nasogastric tubes or wounds left to **heal by secondary intention** (ie, the wound is purposely left open).

**(Choice A)** Cutaneous amyloidosis is caused by the deposition of insoluble fibers derived from precursor proteins (eg, immunoglobulin light chains) into the superficial dermis. It can have a varied gross appearance (eg, macular, nodular, lichenous) but would be characterized histologically by homogenous, **eosinophilic dermal deposits**.

**(Choice B)** During the remodeling phase of wound healing, fibroblasts and type III collagen in granulation

**(Choice B)** During the remodeling phase of wound healing, fibroblasts and type III collagen in granulation tissue are gradually (ie, over weeks to years) replaced with myofibroblasts and type I collagen, forming a scar. Abnormalities in this process result in unchecked production of collagen fibers, forming a hypertrophic scar or **keloid** months after the initial wound.

**(Choice C)** Individuals with a resected squamous cell carcinoma lesion are at risk of developing a secondary lesion at the same site. However, these recurrences typically develop years postresection, and histology would typically show acanthosis, keratinization, and evidence of keratinocyte dysplasia (eg, keratinocytes with pleomorphic nuclei and abundant cytoplasm).

**(Choice D)** Neutrophils are essential to the normal inflammatory response in wound healing; they prevent infection and release cytokines and growth factors that allow wound healing to progress. However, protracted inflammation and excessive release of reactive oxygen species by neutrophils in a wound can cause tissue damage that delays wound healing, resulting in a chronic, nonhealing wound.

### Educational objective:

Fibroblast and vascular proliferation (ie, granulation tissue) induced by vascular endothelial growth factor (VEGF) is essential to normal wound healing. However, if this tissue proliferation becomes excessive (eg, in wounds left to heal by secondary intention), the resulting hypergranulation tissue can impair wound reepithelialization and remodeling.





scar. Abnormalities in this process result in unchecked production of collagen fibers, forming a hypertrophic scar or **keloid** months after the initial wound.

**(Choice C)** Individuals with a resected squamous cell carcinoma lesion are at risk of developing a secondary lesion at the same site. However, these recurrences typically develop years postresection, and histology would typically show acanthosis, keratinization, and evidence of keratinocyte dysplasia (eg, keratinocytes with pleomorphic nuclei and abundant cytoplasm).

**(Choice D)** Neutrophils are essential to the normal inflammatory response in wound healing; they prevent infection and release cytokines and growth factors that allow wound healing to progress. However, protracted inflammation and excessive release of reactive oxygen species by neutrophils in a wound can cause tissue damage that delays wound healing, resulting in a chronic, nonhealing wound.

### Educational objective:

Fibroblast and vascular proliferation (ie, granulation tissue) induced by vascular endothelial growth factor (VEGF) is essential to normal wound healing. However, if this tissue proliferation becomes excessive (eg, in wounds left to heal by secondary intention), the resulting hypergranulation tissue can impair wound reepithelization and remodeling.

Pathophysiology

Dermatology

Wound healing





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A 37-year-old man comes to the office due to a rash. For the last several months, he has had numerous small lesions on the hands. The lesions are associated with occasional mild itching and bleed slightly if inadvertently struck against furniture or a wall. Examination findings are as shown in the [exhibit](#). Which of the following is the most likely diagnosis?

- ☐ A. Atopic dermatitis
- ☐ B. Cutaneous warts
- ☐ C. Lichen planus
- ☐ D. Psoriasis
- ☐ E. Tinea infection

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A 37-year-old man comes to the office due to a rash. For the last several months, he has had numerous small lesions on the hands. The lesions are associated with occasional mild itching and bleed slightly if inadvertently struck against furniture or a wall. Examination findings are as shown in the [exhibit](#). Which of the following is the most likely diagnosis?

- ☐ A. Atopic dermatitis (1%)
- ☐ B. Cutaneous warts (7%)
- ☐ C. Lichen planus (12%)
- ☒ D. Psoriasis (74%)
- ☐ E. Tinea infection (3%)

Correct

 74%  
Answered correctly

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 10/13/2020  
Last Updated

Explanation

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This patient has chronic, well-demarcated, erythematous plaques with a thick scale consistent with **plaque psoriasis**. Psoriasis is a common inflammatory skin disorder characterized by hyperkeratosis (overgrowth of the stratum corneum) and epidermal hyperplasia. It has a strong genetic predisposition and is often seen in patients with a family history of the disorder; other risk factors include smoking, heavy alcohol consumption, and obesity.

Psoriasis has multiple variants (eg, guttate, pustular); however, up to 75% of cases are due to chronic plaque psoriasis. Plaques are well-defined and **erythematous** and may appear raised above the surrounding skin. They are typically covered in a coarse **silver scale**, which, when removed, results in **pinpoint bleeding** (Auspitz sign) of the underlying dilated capillaries.

Plaques usually form in locations subject to trauma or friction (**Köbner phenomenon**); the extensor surfaces of the elbows and knees are most classic, but the dorsal surface of the hands, as in this patient, is also common. Other typical locations include the scalp, back, and gluteal cleft. They are often **mildly pruritic** but may be asymptomatic.

**(Choice A)** Atopic dermatitis can present with erythematous, scaly plaques, but it is more common in **flexural areas**, shows less prominent scaling, and is usually associated with more prominent itching.

**(Choice B)** Cutaneous warts (verruca vulgaris) are caused by human papillomavirus infection and present

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This patient has chronic well-demarcated erythematous plaques with a thick scale consistent with psoriasis.

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**(Choice A)** Atopic dermatitis can present with erythematous, scaly plaques, but it is more common in flexural areas, shows less prominent scaling, and is usually associated with more prominent itching.

**(Choice B)** Cutaneous warts (verruca vulgaris) are caused by human papillomavirus infection and present as discrete, hyperkeratotic papules. Although patients can have multiple warts, numerous scaly plaques are more consistent with psoriasis.

**(Choice C)** Lichen planus presents with pink or purple plaques and papules. It is usually associated with severe pruritis and typically affects the volar surface of the wrists rather than the dorsum of the hands.

**(Choice E)** Tinea manuum presents with scaly plaques on the hands. The lesions are typically very pruritic and often have an annular appearance with central clearing.

### Educational objective:

Psoriasis is a common inflammatory skin disorder characterized by hyperkeratosis (overgrowth of the stratum corneum) and epidermal hyperplasia. Plaque psoriasis is the most common form and presents with chronic, well-demarcated, erythematous plaques with a thick, silver scale.

Pathology

Dermatology

Psoriasis

Subject

System

Topic





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(Choice A) Atopic dermatitis can present with erythematous, scaly plaques, but it is more common in

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(Choice A) Atopic dermatitis can present with erythematous, scaly plaques, but it is more common in

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**(CHOICE A)** Atopic dermatitis can present with erythematous, scaly plaques, but it is more common in

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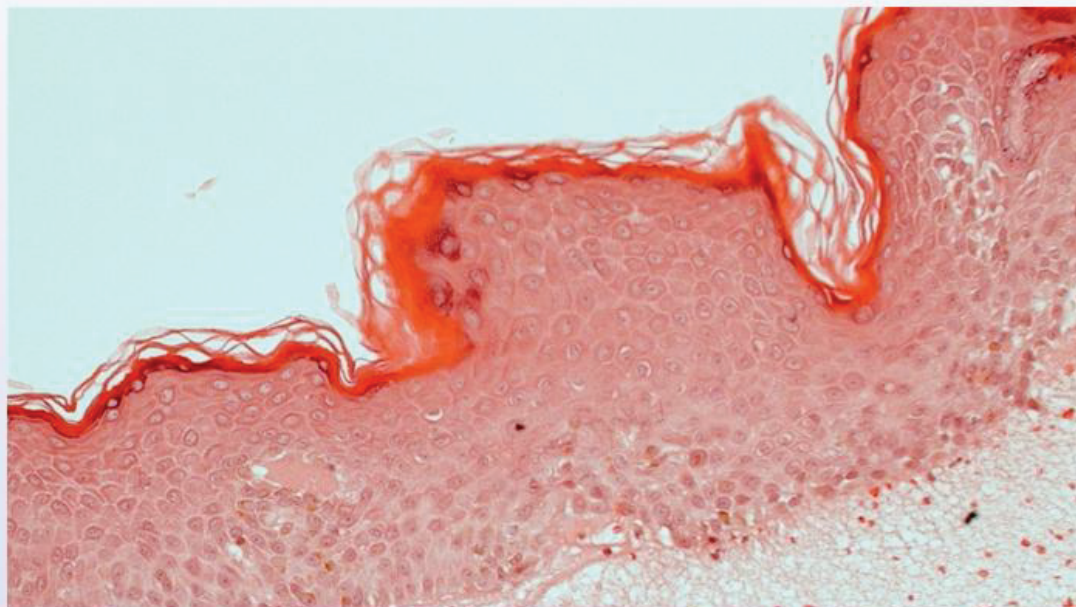
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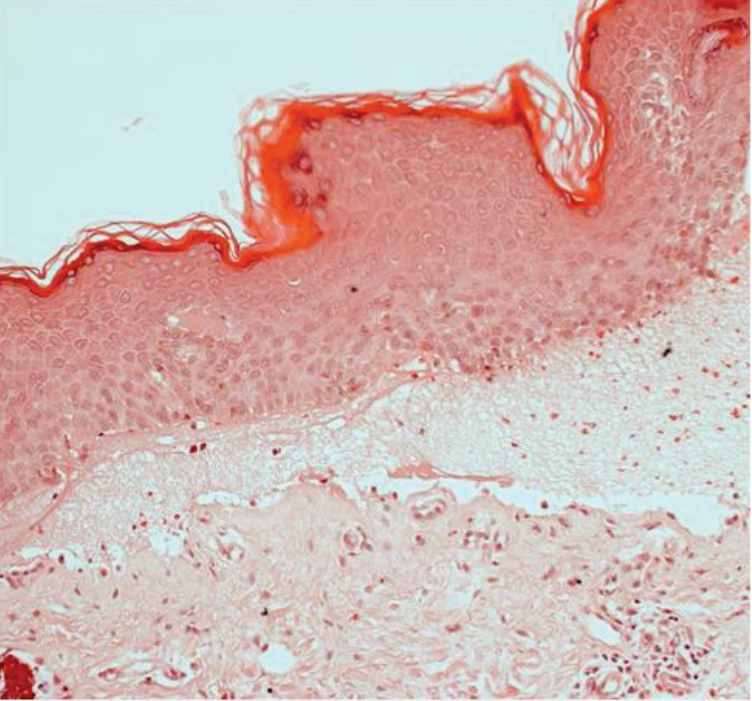
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A 64-year-old man comes to the office due to skin blisters on his trunk and groin. The patient has had itching for the past several weeks and developed the blisters a week ago. He has a history of hypertension and osteoarthritis. The patient received the zoster vaccine at age 60. Examination shows numerous 0.5- to 3-cm bullous skin lesions. The findings from a skin biopsy are shown in the image below.





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Exhibit Display





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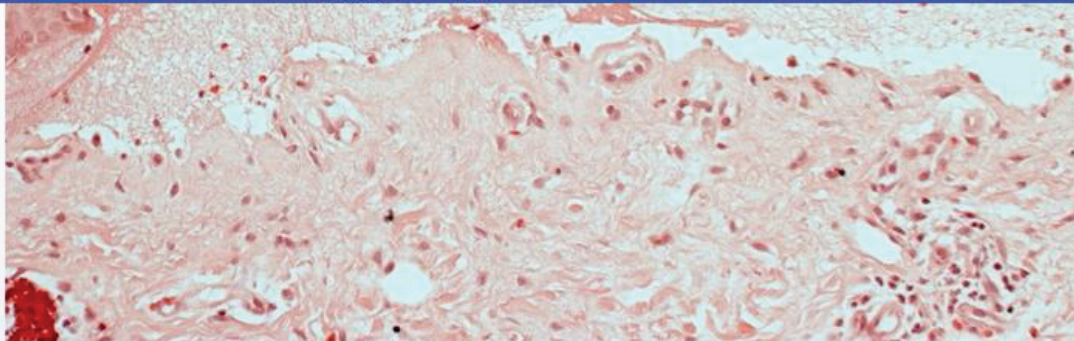
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Which of the following is the most likely diagnosis?

- ☐ A. Bullous pemphigoid
- ☐ B. Contact dermatitis
- ☐ C. Dermatitis herpetiformis
- ☒ D. Lichen planus
- ☐ E. Pemphigus vulgaris

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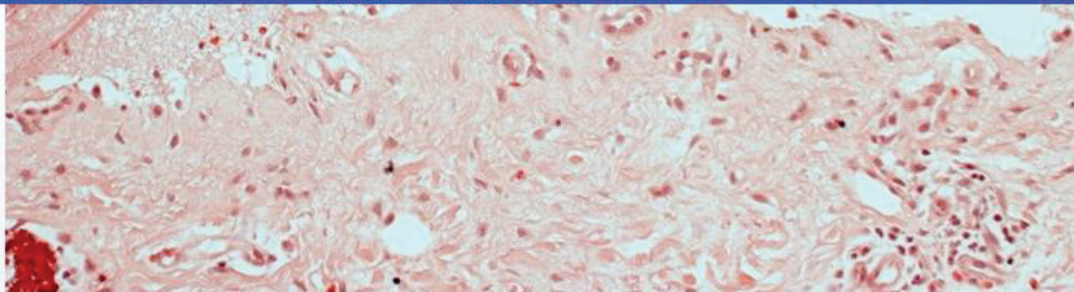
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Which of the following is the most likely diagnosis?

- ✓ ☒ A. Bullous pemphigoid (75%)
- ☐ B. Contact dermatitis (3%)
- ☐ C. Dermatitis herpetiformis (4%)
- ☐ D. Lichen planus (4%)
- ☐ E. Pemphigus vulgaris (11%)

Correct

75%



58 secs



02/18/2021

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	Pemphigus vulgaris	Bullous pemphigoid
Autoantibody target	<ul style="list-style-type: none"><li>Desmosomes (desmogleins 3 &amp; 1)</li></ul>	<ul style="list-style-type: none"><li>Hemidesmosomes (bullous pemphigoid antigens 1 &amp; 2)</li></ul>
Histopathology	<ul style="list-style-type: none"><li>Intraepidermal cleavage</li><li>Acantholysis (detached keratinocytes)</li><li>"Tombstone cells" along basal layer</li></ul>	<ul style="list-style-type: none"><li>Subepidermal cleavage</li><li>No acantholysis</li></ul>
Immunofluorescence	<ul style="list-style-type: none"><li>Net-like intercellular IgG</li></ul>	<ul style="list-style-type: none"><li>Linear IgG at basement membrane</li></ul>
Clinical features	<ul style="list-style-type: none"><li>Middle-aged or elderly</li><li>Flaccid bullae</li><li>Oral/mucosal involvement</li><li>Positive Nikolsky sign</li></ul>	<ul style="list-style-type: none"><li>Predominantly elderly</li><li>Tense bullae</li><li>Rare oral/mucosal involvement</li></ul>

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**Bullous pemphigoid (BP)** is an autoimmune condition characterized by serous fluid-filled, **tense bullae** on normal or erythematous skin. The most common sites of involvement include the inner thighs and flexor aspects of the forearms, axillae, groin, and lower abdomen. Elderly individuals are most commonly affected.

BP is caused by antibodies against **hemidesmosomes** along the basement membrane of the **dermal-epidermal junction**. These autoantibodies result in a destructive inflammatory cascade that causes the entire epidermis to **separate** from the dermis, forming **subepidermal, nonacantholytic blisters**.

Immunofluorescence shows IgG and/or C3 deposits in a linear pattern along the basement membrane.

**(Choice B)** **Acute allergic contact dermatitis** is characterized by localized erythema, vesicles, edema, and severe pruritus. Biopsy typically shows spongiosis (abnormal accumulation of edema fluid in the intercellular spaces between keratinocytes) and lymphocytic perivascular infiltrates.

**(Choice C)** **Dermatitis herpetiformis** is characterized histologically by microabscesses containing fibrin and neutrophils at the dermal papillae tips. The overlying basal cells become vacuolated, and blisters form at the tips of the involved papillae.

**(Choice D)** **Lichen planus** causes pruritic, purple papules and plaques involving the skin and mucous membranes. Microscopic analysis shows a lymphocytic infiltrate at the dermal-epidermal junction with



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Bullous pemphigoid



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membranes. Microscopic analysis shows a lymphocytic infiltrate at the dermal-epidermal junction with

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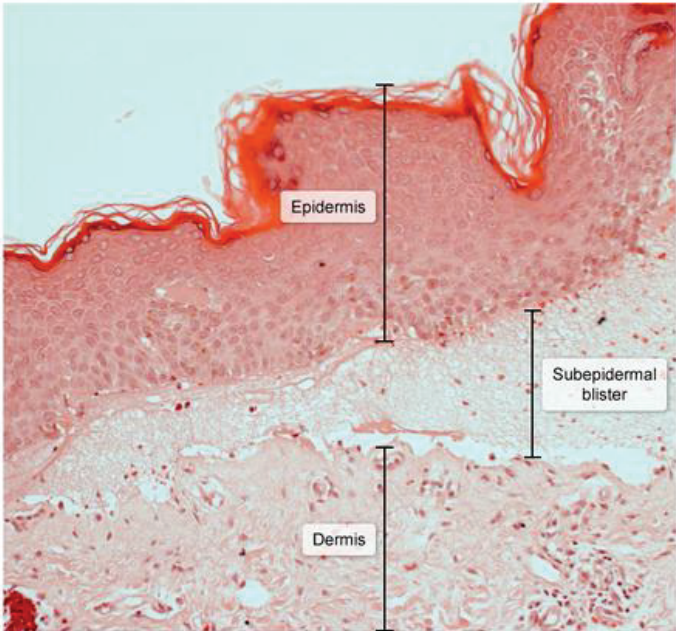
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Bullous pemphigoid



The histological image shows a cross-section of skin with a prominent subepidermal blister. The epidermis is the upper layer, and the dermis is the lower layer. The blister is located between the two layers. Labels indicate the Epidermis, Subepidermal blister, and Dermis.

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membranes. Microscopic analysis shows a lymphocytic infiltrate at the dermal-epidermal junction with

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Acute allergic contact dermatitis



Vesicle (<0.5 cm)

Erythematous, indurated skin

Bulla (>0.5 cm)

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membranes. Microscopic analysis shows a lymphocytic infiltrate at the dermal-epidermal junction with

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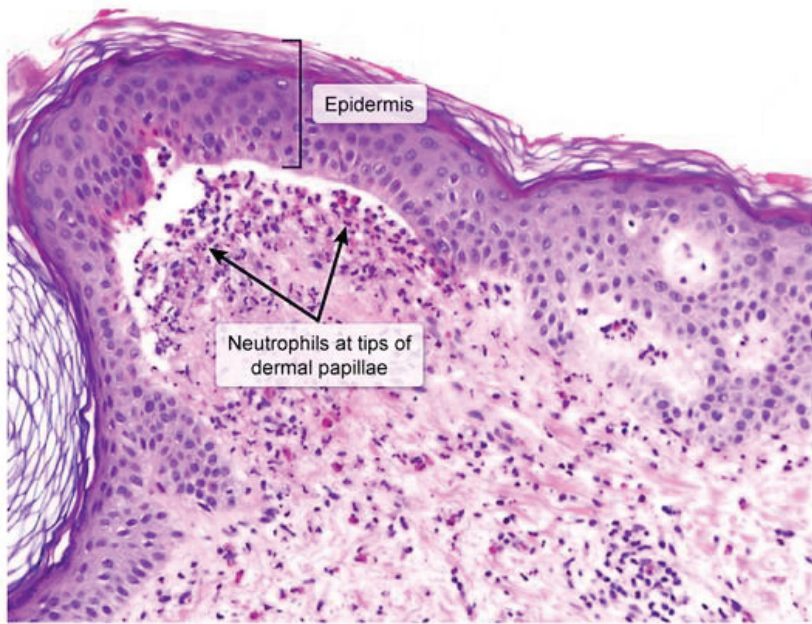
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Dermatitis herpetiformis



Epidermis

Neutrophils at tips of dermal papillae

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membranes. Microscopic analysis shows a lymphocytic infiltrate at the dermal-epidermal junction with

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### Lichen planus

The histological slide shows a cross-section of the epidermis and dermis. The epidermis is thickened, with a prominent granular layer and hyperkeratosis. A band-like lymphocytic inflammation is visible at the dermal-epidermal junction. The rete ridges are saw-toothed. Labels point to the Epidermis, Dermis, Prominent granular layer, Hyperkeratosis, Band-like lymphocytic inflammation, and Saw-toothed rete ridges.

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**(Choice C)** **Dermatitis herpetiformis** is characterized histologically by microabscesses containing fibrin and neutrophils at the dermal papillae tips. The overlying basal cells become vacuolated, and blisters form at the tips of the involved papillae.

**(Choice D)** **Lichen planus** causes pruritic, purple papules and plaques involving the skin and mucous membranes. Microscopic analysis shows a lymphocytic infiltrate at the dermal-epidermal junction with destruction of basal epidermal cells.

**(Choice E)** **Pemphigus** is due to autoantibodies directed against desmosomal proteins. Biopsy of an active pemphigus lesion shows intraepithelial cleavage with detached keratinocytes (acantholysis), retained keratinocytes along the basement membrane, and an eosinophilic inflammatory infiltrate.

**Educational objective:**

Bullous pemphigoid is characterized by autoantibodies against hemidesmosomes along the basement membrane of the dermal-epidermal junction. This causes the entire epidermis to separate from the dermis and form tense, subepidermal blisters.

Pathology

Dermatology

Bullous pemphigoid

Subject

System

Topic

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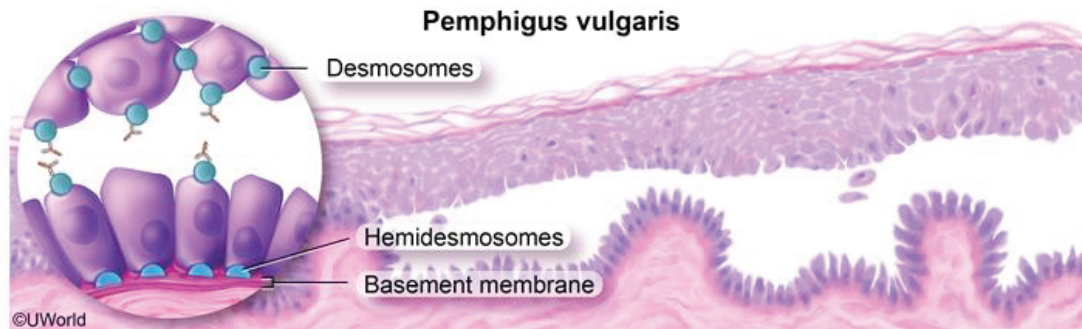
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Settings

(Choice C) Dermatitis herpetiformis is characterized histologically by microabscesses containing fibrin and

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A 31-year-old woman comes to the physician with a velvety skin rash in her axilla, as shown in the image below.



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Which of the following is the most likely cause of this patient's condition?

- ☐ A. Calcitonin hypersecretion
- ☐ B. Insulin resistance
- ☐ C. Serotonin hypersecretion
- ☐ D. Testosterone unresponsiveness
- ☐ E. Vitamin D resistance

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Which of the following is the most likely cause of this patient's condition?

- ☐ A. Calcitonin hypersecretion (1%)
- ☒ B. Insulin resistance (94%)
- ☐ C. Serotonin hypersecretion (2%)
- ☐ D. Testosterone unresponsiveness (0%)
- ☐ E. Vitamin D resistance (0%)

Correct

94%  
Answered correctly

19 secs  
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This image shows the typical presentation of acanthosis nigricans (AN), which occurs most commonly in flexural areas. The most common locations are the axillae, posterior neck, and groin, but it may appear on other areas of the body such as the palms, soles, and oral mucosa & vermilion border. On physical examination, these lesions appear as hyperkeratotic, hyperpigmented plaques with a classic "velvety" texture. **Skin tags** (acrochordons) are pedunculated outgrowths of normal skin that are commonly present on regions affected by acanthosis nigricans.

AN is associated with a number of diseases. Depending on the underlying condition, it is divided into benign and malignant forms.

1. Benign AN is commonly associated with insulin resistance. Increased levels of insulin and insulin-like growth factors stimulate epidermal and dermal proliferation.
2. Malignant AN is associated with underlying neoplasms, especially of the gastrointestinal and genitourinary tracts. The sudden appearance of such skin changes in middle-aged or elderly patients is suggestive of underlying malignancy. Gastric adenocarcinoma is the most common cause of malignant AN.

**(Choices A and E)** Hypersecretion of calcitonin (as in medullary thyroid cancer) and vitamin D resistance are not associated with AN.



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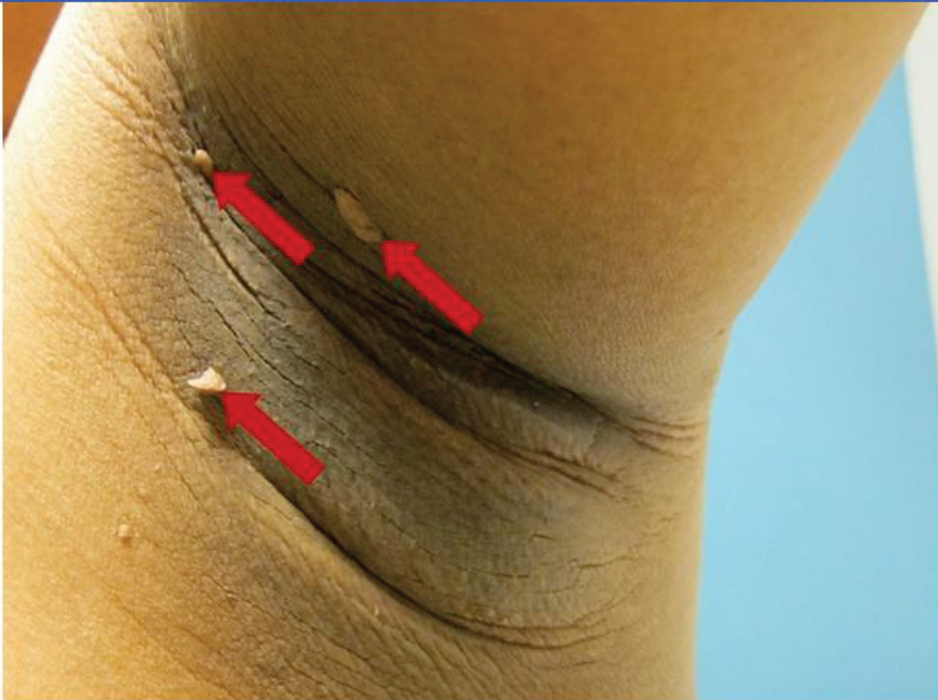
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is suggestive of underlying malignancy. Gastric adenocarcinoma is the most common cause of malignant AN.

**(Choices A and E)** Hypersecretion of calcitonin (as in medullary thyroid cancer) and vitamin D resistance are not associated with AN.

**(Choice C)** Hypersecretion of serotonin can occur with carcinoid tumors, including the gastrointestinal variety. However, excess serotonin itself does not cause AN.

**(Choice D)** Testosterone unresponsiveness (androgen insensitivity syndrome, testicular feminization syndrome) develops due to a defect in testosterone receptors in peripheral tissues. Such patients are phenotypic females who present with primary amenorrhea. The uterus is absent and the vagina ends as a blind pouch, but breast development is normal due to the production of estrogen by aromatase.

### Educational objective:

Acanthosis nigricans presents with thickening and hyperpigmentation of skin in the flexural areas. The lesions have a classic "velvety" texture. Acanthosis nigricans is commonly associated with insulin-resistant states (eg, diabetes mellitus, acromegaly, obesity) and gastrointestinal malignancies.

Pathology

Dermatology

Acanthosis nigricans

Subject

System

Topic

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A 48-year-old man who recently immigrated to the United States comes to the physician with multiple skin lesions. Physical examination shows a few well-defined, hypopigmented lesions on the skin of his lower extremities that have diminished sensation. After confirming the diagnosis of leprosy, the patient undergoes further testing to help classify the severity of his disease. Intradermal injection of heat-killed *Mycobacterium leprae* causes the development of a large indurated nodule. The patient is most likely to demonstrate which of the following additional findings?

- ☐ A. Blood smears positive for mycobacteria
- ☐ B. High serum level of protective antimycobacterial antibodies
- ☐ C. Inactivated macrophages
- ☐ D. Increased interleukin-2 and interferon- $\gamma$  in skin lesions
- ☐ E. Numerous acid-fast bacteria in skin lesions

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A 48-year-old man who recently immigrated to the United States comes to the physician with multiple skin lesions. Physical examination shows a few well-defined, hypopigmented lesions on the skin of his lower extremities that have diminished sensation. After confirming the diagnosis of leprosy, the patient undergoes further testing to help classify the severity of his disease. Intradermal injection of heat-killed *Mycobacterium leprae* causes the development of a large **indurated nodule**. The patient is most likely to demonstrate which of the following additional findings?

- ☐ A. Blood smears positive for mycobacteria (1%)
- ☐ B. High serum level of protective antimycobacterial antibodies (12%)
- ☐ C. Inactivated macrophages (6%)
- ☒ D. Increased interleukin-2 and interferon- $\gamma$  in skin lesions (59%)
- ☐ E. Numerous acid-fast bacteria in skin lesions (18%)

Correct

59%  
Answered correctly

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### Immune response in leprosy

+ lepromin skin test

- lepromin skin test

Cell mediated immunity ( $T_H1$  response)

Humoral immunity ( $T_H2$  response)

Bacterial load

Tuberculoid leprosy

Lepromatous leprosy

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Leprosy is a chronic, slowly progressive, communicable disease caused by *Mycobacterium leprae* that typically involves the skin and peripheral nerves. Clinical manifestations are widely variable depending on the strength of the  $T_H1$  cell-mediated immune response to the organism. Disease is classified along a spectrum between tuberculoid (mild) to lepromatous (severe) forms. Patients with tuberculoid leprosy develop a strong  $T_H1$ -mediated response (interleukin [IL]-2, IFN- $\gamma$ , and IL-12) in affected tissues, leading to the activation of macrophages that kill *M leprae* organisms, thereby limiting disease extent. However, this localized inflammation damages the skin and cutaneous nerves, leading to the development of a small number of hypopigmented, well-demarcated plaques with decreased sensation.

Lepromatous leprosy is a more disseminated form of the disease characterized by an innate inability to recognize and mount a cellular immune response against *M leprae* antigens. Affected tissues show extensive accumulation of acid-fast bacilli within macrophages and often a  $T_H2$  cytokine profile (IL-4, IL-5, and IL-10). Patients with lepromatous leprosy develop more numerous, poorly demarcated plaques that are widespread across the body. Over time, the bacterial load increases and the nodular lesions coalesce, causing the development of leonine facies and degeneration and loss of the nose and digits.

The lepromin skin test (in which *M leprae* antigens are injected intradermally) can be used to distinguish between tuberculoid and lepromatous leprosy. Patients with tuberculoid leprosy will develop an indurated

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The lepromin skin test (in which *M leprae* antigens are injected intradermally) can be used to distinguish between tuberculoid and lepromatous leprosy. Patients with tuberculoid leprosy will develop an indurated nodule at the site of the injection (much like a positive PPD test for *M tuberculosis*). In contrast, the test is usually nonreactive in patients with lepromatous leprosy due to their weak  $T_H1$  cell-mediated immune response.

**(Choice A)** Patients with lepromatous leprosy have a high bacterial load with widespread involvement throughout the peripheral (cooler) tissues of the body. As a result, intermittent bacteremia often occurs in the later stages of the disease. However, this patient's few lesions and positive lepromin skin test are more indicative of tuberculoid leprosy, which has a very low bacterial load with limited tissue involvement.

**(Choice B)** High serum antimycobacterial antibody levels are more frequently seen in lepromatous leprosy than tuberculous leprosy. Because *M leprae* resides mostly within macrophages, circulating immunoglobulins have little access to the organism and are unable to bind, opsonize, or fix complement. Humoral immunity does not influence the positivity of the lepromin skin test.

**(Choice C)** In lepromatous leprosy, macrophages remain inactivated due to the inability of  $T_H1$  cells to recognize *M leprae* antigens. This form of leprosy is characterized by a poor cell-mediated response and diffuse spread of the organism. This patient is presenting with the tuberculoid form, in which activated

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immunoglobulins have little access to the organism and are unable to bind, opsonize, or fix complement. Humoral immunity does not influence the positivity of the lepromin skin test.

**(Choice C)** In lepromatous leprosy, macrophages remain inactivated due to the inability of  $T_H1$  cells to recognize *M leprae* antigens. This form of leprosy is characterized by a poor cell-mediated response and diffuse spread of the organism. This patient is presenting with the tuberculoid form, in which activated macrophages actively kill *M leprae* organisms.

**(Choice E)** Acid-fast bacteria typically do not accumulate in the skin lesions of tuberculoid leprosy due to the strong cell-mediated response that is effective at eradicating *M leprae*. In some instances, this immune response is so effective that tuberculoid leprosy can be self-limited and heal completely without treatment.

**Educational objective:**

The lepromin skin test will be positive in patients with tuberculoid leprosy as they exhibit a strong  $CD4^+$   $T_H1$  cell-mediated immune response to *Mycobacterium leprae*. Patients with lepromatous leprosy will test negative due to their weak  $T_H1$  cell-mediated immune response.

Pathology

Dermatology

Leprosy

Subject

System

Topic

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A 27-year-old woman comes to the emergency department with a scalp laceration after a fall. She reports a tendency to develop big scars even with small injuries. Physical examination reveals an old, healed laceration as shown in the image below.





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Histochemical analysis of her tissue reveals fibroblasts that overexpress a cytokine essential for normal wound healing. Which of the following substances is most likely involved?

- ☐ A. Interferon- $\beta$
- ☐ B. Interleukin-17
- ☐ C. Nuclear factor-kappa B
- ☐ D. Transforming growth factor- $\beta$
- ☐ E. Tumor necrosis factor- $\alpha$



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Histochemical analysis of her tissue reveals fibroblasts that overexpress a cytokine essential for normal wound healing. Which of the following substances is most likely involved?

- ☐ A. Interferon- $\beta$  (1%)
- ☐ B. Interleukin-17 (2%)
- ☐ C. Nuclear factor-kappa B (6%)
- ☒ D. Transforming growth factor- $\beta$  (83%)
- ☐ E. Tumor necrosis factor- $\alpha$  (5%)

Correct

83%



01 min, 42 secs



10/10/2020

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Wound healing generally proceeds in 3 phases:

1. **The inflammatory phase** begins with formation of a fibrin clot that results in hemostasis. Cytokines released by activated platelets and damaged cells lead to migration of neutrophils (within the first 24 hours) and macrophages (2-3 days later) to the damaged area.
2. **The proliferative phase** begins 3-5 days after the injury. Fibroblasts and endothelial vascular cells proliferate to form connective tissue and blood vessels (neovascularization), respectively. Around this time, epithelial cells begin to proliferate at the dermal edges and secrete basement membrane material.
3. **The maturation phase** is characterized by fibrosis (scar formation) and starts during the second week after injury. During this phase, active fibroblasts synthesize collagen, elastin, and other components of the connective tissue matrix.

During the healing process, fibroblast migration and proliferation are controlled by multiple growth factors including platelet-derived growth factor (PDGF) and **transforming growth factor- $\beta$**  (TGF- $\beta$ ). TGF- $\beta$  is also critical for stimulating connective tissue synthesis and remodeling of the extracellular matrix. TGF- $\beta$  typically decreases during the maturation phase of wound healing to limit the amount of collagenous scar tissue. Hypertrophic or disfiguring scars can be caused by persistently elevated TGF- $\beta$ , which leads to



**(Choice E)** Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) is a cytokine secreted by activated macrophages and T cells that promotes leukocyte recruitment, induces the systemic inflammatory response (eg, fever, acute-phase proteins) and regulates apoptosis.



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**(Choice B)** Interleukin-17 (IL-17) is produced by  $T_H17$  cells and recruits neutrophils in addition to

stimulating production of antimicrobial peptides. IL-17 improves host defense against fungi and bacteria at epithelial and mucosal surfaces. Dysregulation has been implicated in many autoimmune conditions.

**(Choice C)** Nuclear factor-kappa B (NF- $\kappa$ B) is a proinflammatory transcription factor that regulates cytokine production, adhesion molecule expression, and cell survival. Increased NF- $\kappa$ B activity is found in many cancers and inflammatory diseases (eg, rheumatoid arthritis, inflammatory bowel disease).

**(Choice E)** Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) is a cytokine secreted by activated macrophages and T cells that promotes leukocyte recruitment, induces the systemic inflammatory response (eg, fever, acute-phase proteins), and regulates apoptosis.

### Educational objective:

Transforming growth factor- $\beta$  (TGF- $\beta$ ) is critical for fibroblast migration, proliferation, and connective tissue synthesis. Increased TGF- $\beta$  activity is responsible for the hypertrophic/keloid scarring and fibrosis of the lung, liver, and kidney that occur with chronic inflammation.

### References

- The role of the TGF- $\beta$  family in wound healing, burns and scarring: a review





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A 35-year-old man comes to the office for evaluation of a rash on his elbows. The patient has had this rash intermittently for several months, but lately, it has become more persistent and bothersome. He has had mild associated itching but no pain and has tried a topical moisturizing lotion without relief. The patient installs tile floors for a residential construction company. He has no chronic medical conditions and takes no regular medications. The patient does not use tobacco, alcohol, or illicit drugs. Vitals signs are within normal limits. The rash on his elbow is shown below, and a similar rash is present on the other elbow.







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Which of the following histologic changes would be most likely if this patient's skin lesion were biopsied?

- ☐ A. Epidermal hyperplasia
- ☐ B. Granulomatous inflammation
- ☐ C. Intense eosinophilic infiltration
- ☐ D. Squamous cell dysplasia
- ☐ E. Thinning of the epidermis

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Which of the following histologic changes would be most likely if this patient's skin lesion were biopsied?

- ☒ A. Epidermal hyperplasia (64%)
- ☐ B. Granulomatous inflammation (3%)
- ☐ C. Intense eosinophilic infiltration (13%)
- ☐ D. Squamous cell dysplasia (1%)
- ☐ E. Thinning of the epidermis (17%)

Correct



01 min, 20 secs



02/22/2021

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Psoriasis

Retained nuclei in stratum corneum (parakeratosis)

Dilated capillaries

Epidermal thickening (acanthosis) with elongated, clubbed rete ridges

Epidermis

Dermis

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This patient has scaly, erythematous plaques consistent with psoriasis. **Psoriasis** is most common in areas exposed to pressure or friction, such as the extensor surfaces of the elbows and knees, and minor trauma can often precipitate the formation of lesions (**Koebner phenomenon**). In predisposed individuals, disruption of the epithelial barrier leads to activation of antigen-presenting dendritic cells and subsequently to a self-reinforcing **inflammatory cascade** characterized by recruitment and activation of T helper cells and **proliferation of keratinocytes**.

On histology, this results in **hyperkeratosis** (thickening of the stratum corneum) and **parakeratosis** (retention of nuclei in the stratum corneum), which produce the characteristic silvery scales seen on gross examination. Additional changes include diffuse **epidermal hyperplasia** (acanthosis), often with elongated and clubbed rete ridges corresponding to the typical erythematous plaques. Perivascular lymphocytes and dilated dermal capillaries are also seen.

**(Choice B)** A granuloma is a localized, nodular, inflammatory structure composed of aggregates of epithelioid macrophages and multinucleated giant cells. They are seen in a variety of infectious (eg, tuberculosis) and autoimmune (eg, sarcoidosis) diseases but are not seen in psoriasis.

**(Choice C)** Eosinophilic infiltrates are a common finding in pemphigus vulgaris, atopic skin diseases (eg, atopic eczema, allergic contact dermatitis), and dermatitis herpetiformis. These disorders generally present with vesicle or bulla formation, fragility of the skin, and often intense itching. Plaques and nodules when



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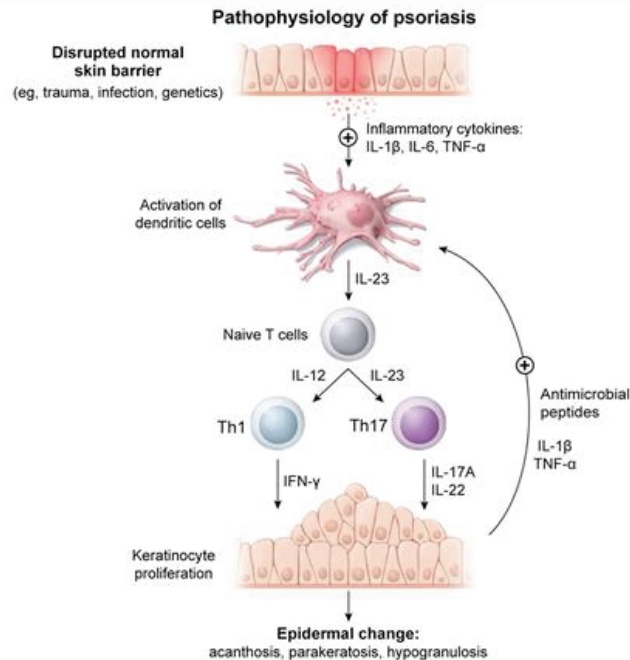
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This patient has scaly, erythematous plaques consistent with psoriasis. Psoriasis is most common in

## Exhibit Display



IFN = interferon; TNF = tumor necrosis factor.

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**(Choice C)** Eosinophilic infiltrates are a common finding in pemphigus vulgaris, atopic skin diseases (eg, atopic eczema, allergic contact dermatitis), and dermatitis herpetiformis. These disorders generally present with vesicle or bulla formation, fragility of the skin, and, often, intense itching. Plaques and scaling, when present, are mainly due to persistent scratching.

**(Choice D)** Actinic keratosis is characterized by hyperkeratosis and squamous dysplasia and is considered a premalignant lesion to squamous cell carcinoma. It is typically related to chronic ultraviolet exposure and is most common on sun-exposed areas of the scalp, ears, face, and dorsum of the hands.


**(Choice E)** Thinning of the epidermis is a common feature of scleroderma. Although patients with psoriasis treated with high-potency corticosteroids can develop skin atrophy over time, it is not a presenting feature of the disorder.

**Educational objective:**

Psoriasis is characterized on histology by hyperkeratosis and confluent parakeratosis of the stratum corneum (producing the characteristic silvery scales seen on gross examination), diffuse epidermal hyperplasia with elongated and clubbed rete ridges (corresponding to the typical erythematous plaques), and dilated capillaries in the dermal papillae.

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A 27-year-old woman comes to the emergency department with a 1-day history of skin rash. Two weeks ago, she had an episode of recurrent genital lesions, which began with small papules and subsequently became vesicular with ulceration, crusting, and eventual healing. The patient has no other medical conditions and takes no medications. On physical examination, she appears comfortable. Temperature is 37 C (98.6 F). She has small linear erosions in the oral mucosa. Skin findings are shown in the image below.





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Which of the following is the most likely diagnosis?

- ☐ A. Disseminated herpes simplex infection
- ☐ B. Erythema multiforme
- ☐ C. Primary HIV infection
- ☐ D. Stevens-Johnson syndrome
- ☐ E. Varicella

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Which of the following is the most likely diagnosis?

☐ A. Disseminated herpes simplex infection (32%)

☒ B. Erythema multiforme (58%)

☐ C. Primary HIV infection (2%)

☐ D. Stevens-Johnson syndrome (5%)

☐ E. Varicella (1%)

Correct

58%

01 min, 16 secs

01/18/2021

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This patient's rash is consistent with **erythema multiforme** (EM), an acute inflammatory disorder that can involve the skin of the extremities, face, trunk, and neck. Severe cases (EM major) can also affect oral mucous membranes and the tongue. The appearance of EM can vary, but patients typically develop erythematous, round papules that evolve into **target lesions** with a dusky central area, a dark red inflammatory zone surrounded by a pale ring, and an erythematous halo in the lesion's periphery.

EM represents a cell-mediated immune process, with an inflammatory infiltrate predominated by cytotoxic CD8<sup>+</sup> lymphocytes. EM is most frequently associated with infections (especially **herpes simplex virus** and mycoplasma) and may be due to an immune response against antigens deposited in the skin. EM can also be seen in association with certain medications (eg, sulfonamides), malignancy, and collagen vascular diseases.

**(Choice A)** Disseminated herpes simplex infection is seen primarily in immunocompromised patients and presents with diffuse vesicles on an erythematous base. EM does not represent disseminated infection, but is a systemic immune response to a localized infection.

**(Choice C)** Primary HIV infection can present with a macular or maculopapular rash associated with fever. The rash is usually well circumscribed and involves the trunk, face, and palms and soles. However, this patient's rash appears more typical of EM.



presents with diffuse vesicles on an erythematous base. EM does not represent disseminated infection, but is a systemic immune response to a localized infection.

**(Choice C)** Primary HIV infection can present with a macular or maculopapular rash associated with fever. The rash is usually well circumscribed and involves the trunk, face, and palms and soles. However, this patient's rash appears more typical of EM.

**(Choice D)** **Stevens-Johnson syndrome** is characterized by rapid onset of erythematous macules with necrosis and skin sloughing. Systemic signs (eg, fever, hypotension) are common. Stevens-Johnson syndrome may also cause target lesions, but it is usually associated with medications (eg, sulfonamides, allopurinol, phenytoin).

**(Choice E)** **Varicella** typically presents with fever and a vesicular eruption that can affect multiple areas, including the face, trunk, abdomen, and extremities. This patient's rash does not have the typical vesicular pattern seen in varicella.

### Educational objective:

Erythema multiforme is a cell-mediated inflammatory disorder of the skin characterized by erythematous papules that evolve into target lesions. It is most commonly associated with herpes simplex virus.

### References



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presents with diffuse vesicles on an erythematous base. EM does not represent disseminated infection.

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A 6mm punch biopsy of normal appearing epidermis reveals stellar cells that contain intracytoplasmic granules having the shape of a tennis racquet. These cells demonstrate some myeloid surface markers and can interact closely with T lymphocytes. The cells described above are best referred to as which of the following?

- ☐ A. Kupffer cells
- ☐ B. Langerhans cells
- ☐ C. Merkel cells
- ☐ D. Melanocytes
- ☐ E. Macrophages
- ☐ F. Epithelioid cells

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A 6mm punch biopsy of normal appearing epidermis reveals stellar cells that contain intracytoplasmic granules having the shape of a tennis racquet. These cells demonstrate some myeloid surface markers and can interact closely with T lymphocytes. The cells described above are best referred to as which of the following?

- ☐ A. Kupffer cells (4%)
- ✓ ☒ B. Langerhans cells (81%)
- ☐ C. Merkel cells (3%)
- ☐ D. Melanocytes (2%)
- ☐ E. Macrophages (4%)
- ☐ F. Epithelioid cells (2%)

Correct

81%  
Answered correctly

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10/04/2020  
Last Updated







**Langerhans cells** (not to be confused with Langhans giant cells, a type of multinucleated cell formed from macrophages) are the form of dendritic cell most commonly found in the skin and mucous membranes.

Dendritic cells are professional **antigen presenting** cells that interact closely with T lymphocytes.

Dendritic are the most effective form of antigen presenting cell because they constitutively express MHC Class II and the co-stimulatory B7 cell surface molecules. They also take up antigen by constant endocytosis and pinocytosis from their environment.

Langerhans cells are derived from the myeloid cell line and express **myeloid** cell surface markers. They contain characteristic "**racquet-shaped**" **intracytoplasmic granules** (Birbeck granules) that are only visible on electron microscopy.

**(Choice A)** Kupffer cells are macrophage-derived cells present in the liver that compose part of the reticuloendothelial system. Kupffer cells lie within the hepatic sinusoids and, like any other macrophage, serve a phagocytic role in the liver.

**(Choice C)** Merkel cells are neuroendocrine cells of the basal layer of the epidermis, often found in association with nerve projections, that play a role in perception of touch. They are associated with a rare but highly malignant form of skin cancer known as Merkel cell carcinoma.





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**(Choice C)** Merkel cells are neuroendocrine cells of the basal layer of the epidermis, often found in association with nerve projections, that play a role in perception of touch. They are associated with a rare but highly malignant form of skin cancer known as Merkel cell carcinoma.

**(Choice D)** Melanocytes are pigment producing cells of the epidermis that arise from the neural crest cells and migrate to the basal layer of the epidermis during embryogenesis. They possess dendritic processes that intercalate between the remaining cells of the epidermis and facilitate the delivery of pigment-laden melanosomes from the melanocyte to the keratinocytes.

**(Choices E and F)** Macrophages can be found in the skin, possess myeloid cell surface markers, and when stimulated, are able to produce dendrite-like extensions of their cytoplasm. Macrophages can also differentiate into multinucleated (Langhans) giant cells and epithelioid cells in the setting of granulomatous inflammation. However, monocytes and their derivatives do not produce Birbeck granules.

### **Educational Objective:**

Langerhans cells are dendritic cells found in the skin that act as professional antigen presenting cells. These cells are derived from the myeloid cell line and they possess characteristic racquet-shaped intracytoplasmic granules known as Birbeck granules.



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A 12-year-old boy is brought to the office due to a week of nonproductive cough and rash. He has also had low-grade fevers, malaise, and headaches. The patient has no prior medical conditions and is up to date with immunizations. Lung examination reveals bilateral crackles and wheezes. There is a diffuse rash on his torso and extremities as shown in the [exhibit](#). Which of the following is the most likely cause of this patient's skin lesions?

- ☐ A. Cytotoxic T-cell-mediated epithelial injury
- ☐ B. Inflammatory reaction in subcutaneous fat
- ☐ C. Keratinocyte hyperproliferation and parakeratosis
- ☐ D. Subepidermal immunoglobulin A deposition
- ☐ E. Vasoactive mediator release from mast cells

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A 12-year-old boy is brought to the office due to a week of nonproductive cough and rash. He has also had low-grade fevers, malaise, and headaches. The patient has no prior medical conditions and is up to date with immunizations. Lung examination reveals bilateral crackles and wheezes. There is a diffuse rash on his torso and extremities as shown in the [exhibit](#). Which of the following is the most likely cause of this patient's skin lesions?

- ✓ ☐ A. Cytotoxic T-cell-mediated epithelial injury (54%)
- ☐ B. Inflammatory reaction in subcutaneous fat (9%)
- ☐ C. Keratinocyte hyperproliferation and parakeratosis (1%)
- ☐ D. Subepidermal immunoglobulin A deposition (13%)
- ✗ ☒ E. Vasoactive mediator release from mast cells (21%)

Incorrect

Correct answer  
A

54%  
Answered correctly

01 min, 29 secs  
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This patient's target-shaped skin lesions likely indicate **erythema multiforme** (EM), an acute, inflammatory skin disorder that usually develops in the setting of an ongoing **infection**. Although herpes simplex virus is the most common trigger, respiratory tract infections due to ***Mycoplasma pneumoniae*** (eg, low-grade fever, headache, fatigue, cough, wheezes) frequently cause EM in children.

EM develops when circulating pathogens are phagocytosed by peripheral mononuclear cells and are brought to the epidermis, where DNA fragments are transferred to keratinocytes via direct cell-to-cell spread (facilitated by upregulation of adhesion molecules). Pathogen-specific **cytotoxic T-cells** then recognize foreign antigens produced by keratinocytes and initiate an inflammatory cascade that results in epithelial damage.

Manifestations of EM include **target-shaped lesions** on the extremities and trunk that have a central dusky area, a surrounding pale ring of edema, and a peripheral halo of erythema. Mucosal lesions also sometimes occur.

**(Choice B)** Erythema nodosum is a delayed-type hypersensitivity reaction that causes inflammatory nodules in the subcutaneous fat. Although it can be triggered by infection, patients generally have tender, erythematous nodules on the bilateral shins (not target-shaped lesions).





erythematous nodules on the bilateral shins (not target-shaped lesions).

**(Choice C)** Psoriasis is an immune-mediated inflammatory disease associated with cytokine-driven keratinocyte hyperproliferation and parakeratosis. It usually causes erythematous, chronic skin plaques with silvery scales on the extensor elbows, scalp, and/or knees.

**(Choice D)** Dermatitis herpetiformis, a manifestation of gluten sensitivity, is caused by the subepidermal deposition of IgA. It is associated with pruritic papules and vesicles on the forearms, knees, and/or scalp (not target-shaped lesions).

**(Choice E)** Urticaria is caused by the release of inflammatory and vasoactive mediators from mast cells in the superficial dermis. Infections (eg, parasites) can cause urticaria, but patients generally have well-circumscribed, raised, pruritic, erythematous plaques. Sometimes the lesions have central pallor, but they are not target-shaped.

### Educational objective:

Erythema multiforme is a target-shaped, inflammatory skin lesion that typically arises in the setting of infection, particularly with herpes simplex virus or *Mycoplasma pneumoniae*. It is caused by the deposition of infectious antigens in keratinocytes, leading to a strong cell-mediated (eg, cytotoxic T-cell) immune response.



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Salmon-colored scaly plaque

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A 47-year-old woman comes to the office due to an itchy rash. For the last 3 months, she has had a gradual onset of multiple pruritic lesions at her wrists, legs, and ankles. The patient tried treating the lesions with emollients and topical over-the-counter hydrocortisone but had no relief. Examination shows scattered, scaly, pink papules and plaques as shown in the [exhibit](#). Which of the following is the most likely diagnosis?

- ☐ A. Actinic keratosis
- ☐ B. Atopic dermatitis
- ☐ C. Irritant contact dermatitis
- ☐ D. Lichen planus
- ☐ E. Psoriasis

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A 47-year-old woman comes to the office due to an itchy rash. For the last 3 months, she has had a gradual onset of multiple pruritic lesions at her wrists, legs, and ankles. The patient tried treating the lesions with emollients and topical over-the-counter hydrocortisone but had no relief. Examination shows scattered, scaly, pink papules and plaques as shown in the [exhibit](#). Which of the following is the most likely diagnosis?

- ☐ A. Actinic keratosis (3%)
- ☐ B. Atopic dermatitis (6%)
- ☐ C. Irritant contact dermatitis (8%)
- ☒ D. Lichen planus (68%)
- ☐ E. Psoriasis (12%)

Correct

68%  
Answered correctly

32 secs  
Time Spent

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<b>Lichen planus</b>	
<b>Clinical findings</b>	<ul style="list-style-type: none"><li>• <b>5 "Ps"</b>: pruritic, purple/pink, polygonal, papules &amp; plaques</li><li>• Lacy, white network of lines (Wickham striae)</li><li>• <b>Locations</b>:<ul style="list-style-type: none"><li>◦ Skin (eg, ankles, wrists)</li><li>◦ Oral mucosa (white papules &amp; plaques ± erythema, mucosal atrophy, ulcers)</li><li>◦ Genitalia</li></ul></li></ul>
<b>Pathologic findings</b>	<ul style="list-style-type: none"><li>• Hyperkeratosis</li><li>• Lymphocytic interface dermatitis</li><li>• Eosinophilic colloid (Civatte) bodies</li><li>• Thickened stratum granulosum, sawtooth rete ridges</li></ul>
<b>Natural history</b>	<ul style="list-style-type: none"><li>• Chronic symptoms</li><li>• Formation of lesions at sites of trauma (Köbner phenomenon)</li><li>• Resolution within 2 yr (mucosal lesions may persist/recur)</li></ul>

This patient has **lichen planus (LP)**, an immune-mediated condition that typically presents with **pruritic**,



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- Resolution within 2 yr (mucosal lesions may persist/recur)

This patient has **lichen planus (LP)**, an immune-mediated condition that typically presents with **pruritic, pink papules** and plaques. LP lesions often have lacy, scaly, **white markings (Wickham striae)** and can form at sites of minor trauma (Köbner phenomenon). The skin lesions typically occur symmetrically on the flexural surfaces of the wrists and ankles but can also involve the nails, oral mucous membranes, and genitalia.

The pathologic process in LP is characterized by a (CD8<sup>+</sup>) **T cell-mediated response** against cells along the **dermal-epidermal junction**. Although the etiology is unknown, the risk may be increased in patients with hepatitis C and those taking certain medications (eg, ACE inhibitors, thiazide diuretics). LP typically follows a chronic course with gradual, spontaneous remission within 2 years.

**(Choice A)** **Actinic keratosis** presents with small, hyperkeratotic plaques in sun-exposed areas (eg, forehead, cheeks). It is most common in patients age >60, and itching is atypical.

**(Choice B)** **Atopic dermatitis** typically occurs in large patches at the flexural surfaces of the extremities, especially the elbows; it usually presents in childhood, and most patients have a history of other atopic disorders (eg, allergic rhinitis, asthma).



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Lichen planus

Pruritic, purple/pink, polygonal papules/plaques



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Exhibit Display

Lichen planus



Lacy, scaly, white markings  
(Wickham striae)

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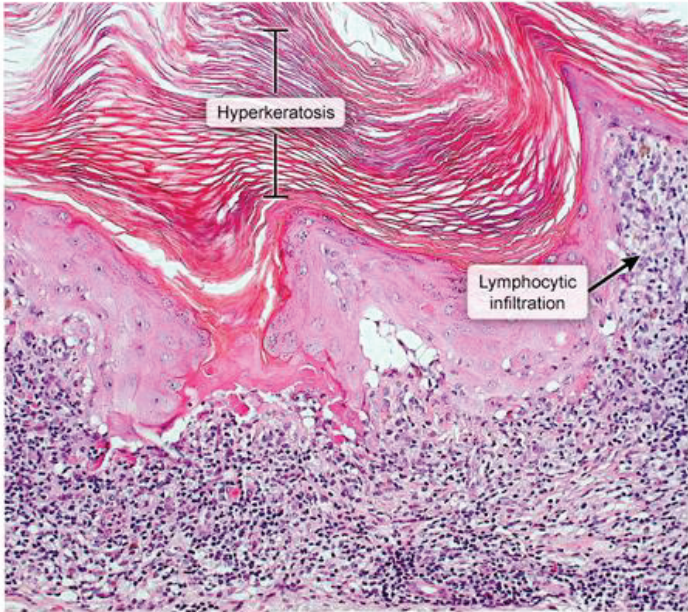
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Lichen planus



Hyperkeratosis

Lymphocytic infiltration

Epidermis

Dermis

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Actinic keratosis



Hyperkeratotic plaque-like lesion in sun-exposed area

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Atopic dermatitis



Pruritic, erythematous patches over flexural surfaces

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especially the elbows; it usually presents in childhood, and most patients have a history of other atopic disorders (eg, allergic rhinitis, asthma).

**(Choice C)** [Irritant contact dermatitis](#) is due to repeated exposure to irritants (eg, detergents, solvents, oxidizing agents). It presents as hyperkeratotic patches with fissuring and scaling, most commonly on the hands.

**(Choice E)** [Psoriasis](#) is an immune-mediated inflammatory disease that usually presents with thick, erythematous plaques with silvery scales on the extensor surfaces of the knees and elbows, scalp, or neck.

### Educational objective:

Lichen planus is an immune-mediated condition that presents with pruritic, pink papules and plaques, often with lacy, scaly, white markings (Wickham striae). The lesions typically occur on the flexural surfaces of the wrists and ankles but can also involve the nails, oral mucous membranes, and genitalia.

### References

- [Update on lichen planus and its clinical variants.](#)

Pathology	Dermatology	Lichen planus
Subject	System	Topic

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Irritant contact dermatitis



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Psoriasis vulgaris



Erythematous plaques with a silvery scale

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A 56-year-old man is brought to the emergency department with new-onset tonic-clonic seizures. His past medical history is unremarkable. The patient recently has had right-sided headaches and has taken acetaminophen with some relief. MRI of the brain reveals several round lesions in the right temporal lobe. After initial evaluation, a stereotactic biopsy of one of the lesions is performed. The biopsy results show neoplastic tissue containing a mutation in the gene that encodes BRAF, a protein kinase. The point mutation results in a valine → glutamic acid substitution at position 600 of the protein. Which of the following is the most likely diagnosis?

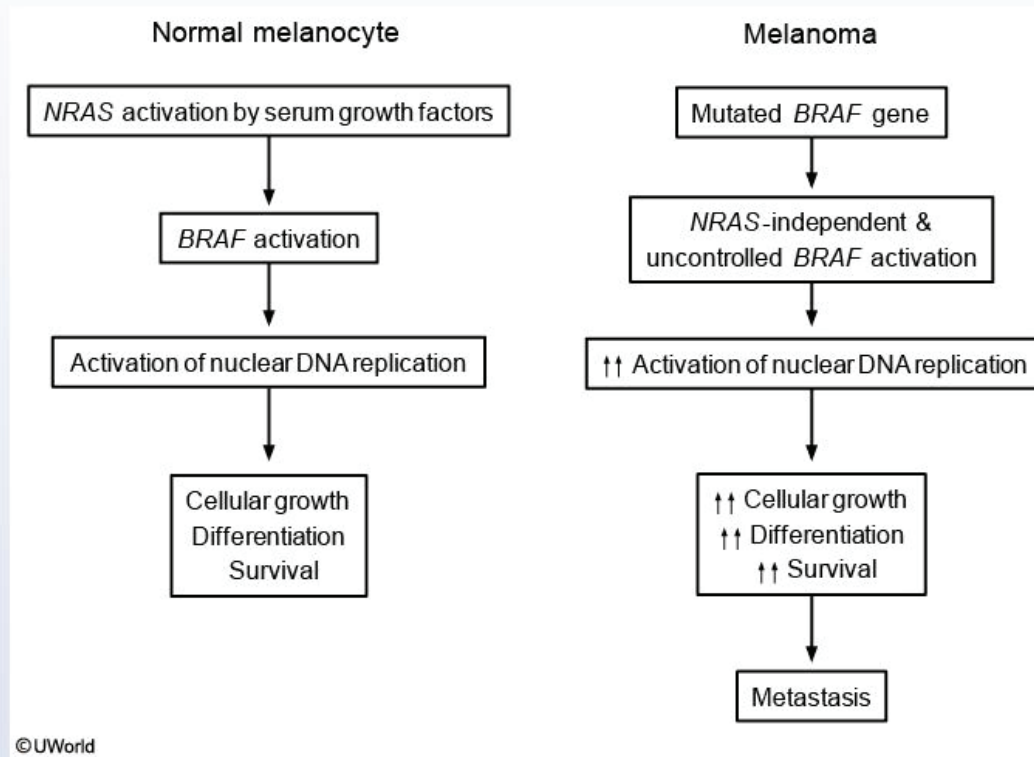
- ☐ A. Glioblastoma
- ☐ B. Melanoma
- ☐ C. Prostate cancer
- ☐ D. Renal cell carcinoma
- ☐ E. Small cell lung cancer

Submit



A 56-year-old man is brought to the emergency department with new-onset tonic-clonic seizures. His past medical history is unremarkable. The patient recently has had right-sided headaches and has taken acetaminophen with some relief. MRI of the brain reveals several round lesions in the right temporal lobe. After initial evaluation, a stereotactic biopsy of one of the lesions is performed. The biopsy results show neoplastic tissue containing a mutation in the gene that encodes **BRAF**, a protein kinase. The point mutation results in a valine → glutamic acid substitution at position 600 of the protein. Which of the following is the most likely diagnosis?

- ☐ A. Glioblastoma (10%)
- ☒ B. Melanoma (69%)
- ☐ C. Prostate cancer (4%)
- ☐ D. Renal cell carcinoma (5%)
- ☐ E. Small cell lung cancer (9%)

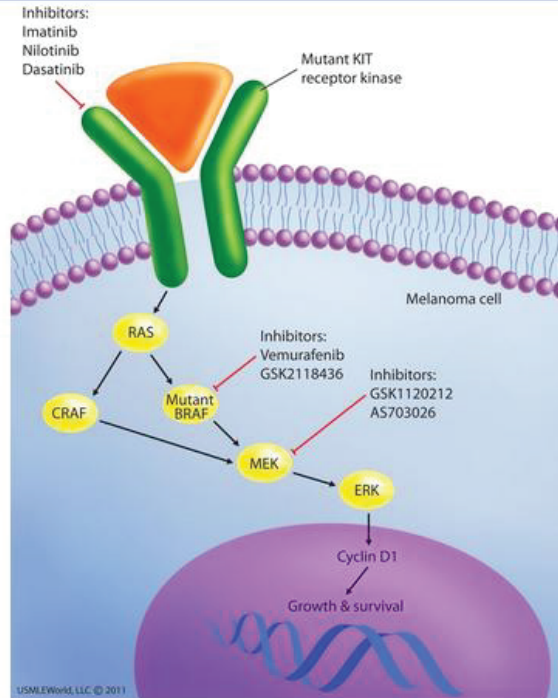


The main environmental risk factor for cutaneous melanoma is increased exposure to ultraviolet radiation.





### Exhibit Display



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**(Choice A)** Glioblastoma is more likely to present as a single lesion; *BRAF* mutations are less common than with melanoma.

**(Choice C)** Prostate cancer is associated with *BRCA1* and *BRCA2* mutations, not *BRAF* mutations. *BRCA* mutations also increase the risk of breast cancer.

**(Choices D and E)** Renal cell carcinoma and small cell lung cancer appear to be multifactorial in origin, involving many different genes and environmental factors. However, *BRAF* has not been associated with either malignancy.

### Educational objective:

*BRAF* is a protein kinase involved in activation of signaling pathways for melanocyte proliferation; the *BRAF* V600E mutation is seen in 40%-60% of patients with melanoma.

### References

- Improved survival with vemurafenib in melanoma with *BRAF* V600E mutation.
- Incidence of the V600K mutation among melanoma patients with *BRAF* mutations, and potential therapeutic response to the specific *BRAF* inhibitor PLX4032.



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A 45-year-old man comes to the office due to recurrent, painful skin lesions in the right axilla for the past 6 months. The patient has no other medical history and takes no medication. He smokes a pack of cigarettes every day and works as a roofer. Vital signs are normal. Examination reveals tender, subcutaneous nodules in the right axilla and other findings as shown in the [exhibit](#). The remainder of the examination is normal. Which of the following is the most likely cause of the condition?

- ☐ A. Bacterial proliferation in eccrine sweat glands
- ☐ B. Immune response to *Cutibacterium acnes*
- ☐ C. Malignant transformation of epithelial cells
- ☐ D. Obstruction of folliculopilosebaceous units

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A 45-year-old man comes to the office due to recurrent, painful skin lesions in the right axilla for the past 6 months. The patient has no other medical history and takes no medication. He smokes a pack of cigarettes every day and works as a **roofer**. Vital signs are normal. Examination reveals tender, subcutaneous nodules in the right axilla and other findings as shown in the [exhibit](#). The remainder of the examination is normal. Which of the following is the most likely cause of the condition?

- ☒ A. Bacterial proliferation in eccrine sweat glands (33%)
- ☐ B. Immune response to *Cutibacterium acnes* (7%)
- ☐ C. Malignant transformation of epithelial cells (22%)
- ☒ D. Obstruction of folliculopilosebaceous units (36%)

**Incorrect**

Correct answer  
D

 36%  
Answered correctly

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Explanation

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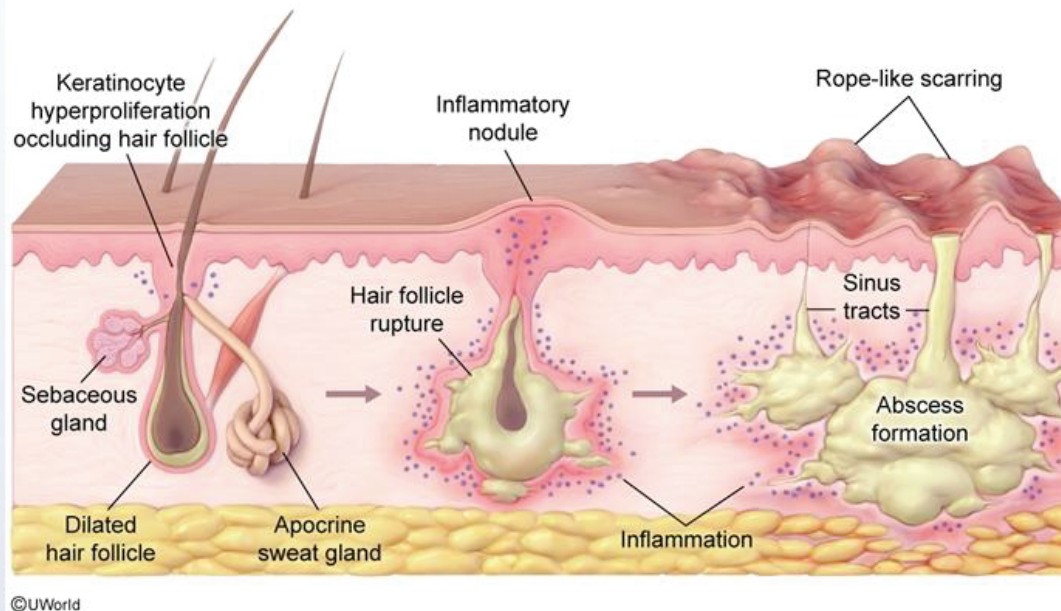
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### Pathogenesis of hidradenitis suppurativa



This patient has **hidradenitis suppurativa** (HS), which is characterized by painful, deep-seated nodules and scar formation in the **axillae**, **groin**, and **medial thighs**. The pathogenesis of HS begins with the **occlusion of folliculopilosebaceous units** caused by keratinocyte hyperproliferation and abnormal

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hair follicle

sweat gland

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This patient has **hidradenitis suppurativa** (HS), which is characterized by painful, deep-seated nodules and scar formation in the **axillae, groin, and medial thighs**. The pathogenesis of HS begins with the **occlusion of folliculopilosebaceous units** caused by keratinocyte hyperproliferation and abnormal keratinocyte differentiation. Mechanical stress (eg, friction in intertriginous areas) then leads to follicular rupture and the release of proinflammatory contents. Contributing factors include tobacco use, immune dysregulation, hormonal factors (eg, excessive androgen effect), and bacterial colonization/infection.

HS is a **chronic, recurring** condition with progressive formation of **draining abscesses, sinus tracts** (formed by epithelial stem cells released from follicular rupture), comedones (from significant follicular damage), and extensive **fibrosis**. In contrast to common furuncles and carbuncles, which usually resolve completely with drainage and antibacterial therapy, HS may persist and recur despite months of antibiotic therapy.

**(Choice A)** It was once thought that HS is a suppurative disease involving the apocrine, not the eccrine, sweat glands. However, current understanding supports follicular occlusion as the cause.

**(Choice B)** Colonization of hair follicles by *Cutibacterium acnes* triggers the inflammatory response seen in acne vulgaris, which typically begins in adolescence and primarily affects the face, chest, and upper

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therapy.

**(Choice A)** It was once thought that HS is a suppurative disease involving the apocrine, not the eccrine, sweat glands. However, current understanding supports follicular occlusion as the cause.

**(Choice B)** Colonization of hair follicles by *Cutibacterium acnes* triggers the inflammatory response seen in acne vulgaris, which typically begins in adolescence and primarily affects the face, chest, and upper back. In contrast, HS involves the intertriginous regions, with symptoms usually beginning after age 18. Early HS lesions are typically sterile but later become colonized or infected with gram-positive, gram-negative, and anaerobic bacteria.

**(Choice C)** Squamous cell carcinoma can occasionally arise in areas affected by HS due to chronic inflammation. However, it typically presents as a well-demarcated, **scaly papule** or plaque, features absent in this patient's lesion.

**Educational objective:**

Hidradenitis suppurativa results from the occlusion of folliculopilosebaceous units. Subsequent follicular rupture and inflammation form painful nodules and abscesses, which may progress to sinus tracts, scars, and comedones with chronic, recurrent disease.

## References



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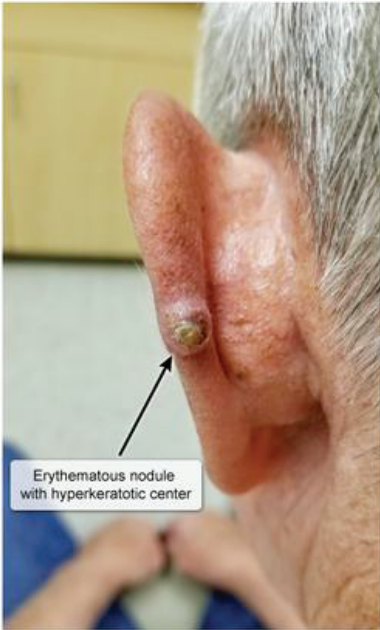
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therapy.

Exhibit Display

Squamous cell carcinoma



Erythematous nodule with hyperkeratotic center

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A 2-week-old boy has an elevated lesion over the genital area as seen in the image below:



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Which of the following is the most likely natural course of this lesion?

- ☐ A. First increase and then regress in size
- ☐ B. First regress and then increase in size
- ☐ C. Progressively increase in size
- ☐ D. Progressively regress in size
- ☐ E. Remain stable in size

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Which of the following is the most likely natural course of this lesion?

- ☒ A. First increase and then regress in size (64%)
- ☐ B. First regress and then increase in size (0%)
- ☐ C. Progressively increase in size (2%)
- ☐ D. Progressively regress in size (29%)
- ☐ E. Remain stable in size (2%)

Correct

64%  
Answered correctly

25 secs  
Time Spent

11/02/2020  
Last Updated

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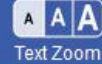
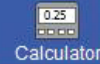
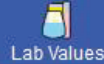
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### Infantile hemangioma

<b>Pathology</b>	<ul style="list-style-type: none"><li>• Benign proliferation of endothelial cells</li><li>• Lobules of densely packed capillaries</li></ul>
<b>Natural history</b>	<ul style="list-style-type: none"><li>• Appears days to weeks after birth</li><li>• Proliferation in infancy<ul style="list-style-type: none"><li>◦ Bright red, raised plaques</li><li>◦ Soft, compressible, well-demarcated</li></ul></li><li>• Involution &amp; regression in size through early childhood</li></ul>
<b>Management</b>	<ul style="list-style-type: none"><li>• Observation if uncomplicated (ie, no ulceration or vision/airway obstruction)</li></ul>

This child has an **infantile hemangioma**, a common, **benign vascular tumor** composed of closely packed capillaries.

Infantile hemangiomas are not usually apparent at birth and typically present in the first few days to weeks of life as **bright red, raised, and sharply demarcated plaques**. They can arise anywhere in the body and usually occur as a single lesion on the skin and subcutaneous tissue. Less commonly, multiple cutaneous hemangiomas may be present, increasing the risk for visceral (eg, hepatic) lesions.





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hemangiomas may be present, increasing the risk for visceral (eg, hepatic) lesions.

The natural progression of hemangiomas begins with **proliferation** in infancy due to growth of blood vessels within the hemangioma. Following the proliferative phase, an **involution** phase occurs, in which the lesion spontaneously regresses (**Choice B**). During involution, the hemangioma dulls in color and softens, eventually resulting in complete resolution in early childhood in most cases.

(**Choice C**) **Port-wine stain**, or nevus flammeus, is a capillary malformation that begins as a flat, unilateral pink patch that grows proportionally with the child and may evolve into a deep purple, thickened, nodular lesion. Port-wine stains do not regress in size.

(**Choice D**) Nevus simplex is a flat, pink, blanching vascular lesion that commonly occurs on the eyelids, forehead, and nape of the neck. These lesions are benign and typically regress in early childhood.

(**Choice E**) A **cherry angioma** is a vascular lesion characterized by a proliferation of capillaries that remain stable in size. However, this lesion is typically small (<0.5 cm) and develops in older adults, not infants.

### Educational objective:

Infantile hemangioma is a common, benign vascular tumor that presents soon after birth as a bright red, raised, sharply demarcated plaque. The natural course of hemangiomas is proliferation in infancy followed







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## Common vascular lesions in childhood

Nevus flammeus  
(port-wine stain)

- Red to purple patches that do not regress
- Respect midline

Nevus simplex



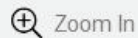
- Blanching pink patches that fade with time
- Usually located on eyelids, glabella, and nape of neck

Hemangioma

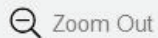


- Bright red raised plaque
- Undergoes proliferation followed by involution

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the lesion spontaneously regresses (Choice B). During involution, the hemangioma dims in color and

softens, eventually resulting in complete resolution in early childhood in most cases.

**(Choice C)** Port-wine stain, or nevus flammeus, is a capillary malformation that begins as a flat, unilateral pink patch that grows proportionally with the child and may evolve into a deep purple, thickened, nodular lesion. Port-wine stains do not regress in size.

**(Choice D)** Nevus simplex is a flat, pink, blanching vascular lesion that commonly occurs on the eyelids, forehead, and nape of the neck. These lesions are benign and typically regress in early childhood.

**(Choice E)** A cherry angioma is a vascular lesion characterized by a proliferation of capillaries that remain stable in size. However, this lesion is typically small (<0.5 cm) and develops in older adults, not infants.

### Educational objective:

Infantile hemangioma is a common, benign vascular tumor that presents soon after birth as a bright red, raised, sharply demarcated plaque. The natural course of hemangiomas is proliferation in infancy followed by regression in early childhood.

### References

- [Hemangioma.](#)





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A 65-year-old man comes to the office due to fatigue, decreased appetite, and weight loss. He has lost 5.4 kg (12 lb) over the last 3 months and eats only small portions of food because he feels full soon after he begins eating. The patient smokes a pack of cigarettes per day and drinks alcohol socially. Blood pressure is 152/90 mm Hg and pulse is 90/min. Physical examination shows a firm, 3-cm lymph node above the left clavicle. There are also numerous skin lesions on his trunk, as shown below, which the patient notes have developed since the onset of his other symptoms.



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This patient's skin lesions most likely represent which of the following conditions?

- ☐ A. Acanthosis nigricans
- ☐ B. Malignant melanoma
- ☐ C. Neurofibromatosis
- ☐ D. Psoriasis
- ☐ E. Seborrheic keratosis
- ☐ F. Tuberous sclerosis

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This patient's skin lesions most likely represent which of the following conditions?

☐ A. Acanthosis nigricans (3%)

☐ B. Malignant melanoma (2%)

☐ C. Neurofibromatosis (20%)

☐ D. Psoriasis (0%)

☒ E. Seborrheic keratosis (70%)

☐ F. Tuberous sclerosis (3%)

Correct

70%

01 min, 57 secs

02/26/2021

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Skin conditions & associated diseases	
Skin conditions	Important associated conditions
<ul style="list-style-type: none"><li>• Acanthosis nigricans</li><li>• Multiple skin tags</li></ul>	<ul style="list-style-type: none"><li>• Insulin resistance</li></ul>
<ul style="list-style-type: none"><li>• Porphyria cutanea tarda</li><li>• Cutaneous leukocytoclastic vasculitis (palpable purpura) secondary to cryoglobulinemia</li></ul>	<ul style="list-style-type: none"><li>• Hepatitis C</li></ul>
<ul style="list-style-type: none"><li>• Dermatitis herpetiformis</li></ul>	<ul style="list-style-type: none"><li>• Celiac disease</li></ul>
<ul style="list-style-type: none"><li>• Recurrent herpes zoster</li><li>• Disseminated molluscum contagiosum</li></ul>	<ul style="list-style-type: none"><li>• Immunosuppression</li></ul>
<ul style="list-style-type: none"><li>• Explosive onset of numerous seborrheic keratoses</li></ul>	<ul style="list-style-type: none"><li>• Gastrointestinal malignancy</li></ul>
<ul style="list-style-type: none"><li>• Pyoderma gangrenosum</li></ul>	<ul style="list-style-type: none"><li>• Inflammatory bowel disease</li></ul>

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This patient's weight loss, early satiety, positive smoking history, and left supraclavicular adenopathy are concerning for **gastric adenocarcinoma** (GA). Patients with GA can also have epigastric pain, hematemesis, and occult blood loss in the stool. Physical examination findings in advanced (metastatic) disease include left supraclavicular (Virchow node) or left axillary lymphadenopathy, or a periumbilical mass (Sister Mary Joseph nodule).

In addition, **rapid onset of numerous seborrheic keratoses** (pigmented macules or plaques with a greasy surface and well-demarcated borders) is a classic **indicator of internal malignancy** (Leser-Trélat sign), particularly GA, and is thought to occur in response to increased tumor production of cytokines or growth factors (eg, IGF-1, fibroblast growth factor). **Acanthosis nigricans** (a hyperpigmented skin disorder typically associated with insulin resistance) can also occur in malignancy due to a similar mechanism **(Choice A)**.

**(Choice B)** **Melanoma** characteristically presents as an asymmetric, pigmented lesion with an irregular border, variable coloration, and change in size and appearance over time. Lesions that are multifocal, monotonous, and otherwise asymptomatic are more typical of seborrheic keratoses.

**(Choice C)** Cutaneous neurofibromas are soft, mobile tumors that are occasionally hyperpigmented. They are often solitary and sporadic, although numerous lesions may occur in **neurofibromatosis** types 1 and 2.



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monotonous, and otherwise asymptomatic are more typical of seborrheic keratoses.

**(Choice C)** Cutaneous neurofibromas are soft, mobile tumors that are occasionally hyperpigmented. They are often solitary and sporadic, although numerous lesions may occur in **neurofibromatosis** types 1 and 2. However, these inherited disorders typically present in childhood or young adulthood, and type 1 (the more common type) is also characterized by axillary freckling, café-au-lait macules, and iris hamartomas.

**(Choice D)** **Psoriasis** is an inflammatory dermatosis characterized by well-demarcated plaques with silvery scales. It can affect the trunk but is more common on extensor surfaces of the extremities. Explosive onset of psoriasis is associated with HIV infection.

**(Choice F)** Tuberous sclerosis is an inherited neurocutaneous syndrome. Cutaneous findings include hypopigmented macules, periungual fibromas, connective tissue nevi, forehead fibrous plaques, and **facial angiofibromas**.

### Educational objective:

Seborrheic keratoses are pigmented macules or plaques with a greasy surface and well-demarcated borders. Rapid onset of numerous lesions is an indicator of internal malignancy (Leser-Trélat sign), especially gastric adenocarcinoma.

Pathology Dermatology Seborrheic keratosis

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monotonous, and otherwise asymptomatic are more typical of seborrheic keratoses.

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monotonous, and otherwise asymptomatic are more typical of seborrheic keratoses.

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monotonous, and otherwise asymptomatic are more typical of seborrheic keratoses.

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Which of the following is the most likely diagnosis?

- ☐ A. Actinic keratosis
- ☐ B. Atopic dermatitis
- ☐ C. Pityriasis rosea
- ☐ D. Psoriasis
- ☐ E. Seborrheic keratosis

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Which of the following is the most likely diagnosis?

✓

☒

A. Actinic keratosis (82%)

☐

B. Atopic dermatitis (3%)

☐

C. Pityriasis rosea (1%)

☐

D. Psoriasis (3%)

☐

E. Seborrheic keratosis (9%)

Correct

82%

14 secs

12/24/2020

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This patient has **actinic keratoses (AKs)**, which most commonly present as **erythematous papules** with overlying **whitish scale**. They are often "felt more than seen" and have a rough, **sandpaper-like texture** on palpation. The lesions are small and flat at first, but may enlarge and become elevated. Usually their size does not exceed 10 mm in diameter. Hyperkeratosis in such lesions may become prominent and form **cutaneous horns**.

AKs develop in genetically predisposed individuals age 40-60 under the influence of **excessive sun exposure**. The most commonly affected areas are the face, ears, scalp, and the dorsa of the arms and hands, but any other chronically sun-exposed site (legs, back, upper chest) can be involved. AK is regarded as a **premalignant condition**, but less than 1% of AKs per year will evolve into invasive squamous cell carcinoma.

**(Choice B)** **Acute atopic dermatitis** occurs most often in infants and children and manifests with highly pruritic erythematous papules and plaques. Light microscopy demonstrates spongiosis (edema of the epidermis).

**(Choice C)** Pityriasis rosea often begins as a solitary pink or brown scaly plaque with central clearing on the trunk, neck, or extremities (herald patch). It is followed by development of an ovoid maculopapular rash with lesions classically oriented in an oblique direction along the skin tension lines on the back (**Christmas**

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Cutaneous horns

Cutaneous horns



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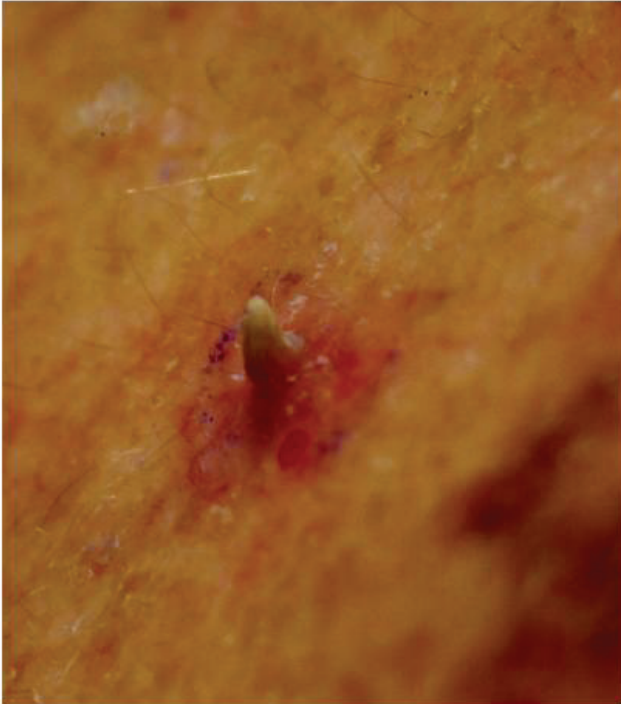
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Cutaneous horns [Cutaneous horns](#)



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Severe eczema exacerbation

Eczema (atopic dermatitis)



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pruritic erythematous papules and plaques. Light microscopy demonstrates spongiosis (edema of the epidermis).

**(Choice C)** Pityriasis rosea often begins as a solitary pink or brown scaly plaque with central clearing on the trunk, neck, or extremities (herald patch). It is followed by development of an ovoid maculopapular rash with lesions classically oriented in an oblique direction along the skin tension lines on the back (**Christmas tree pattern**).

**(Choice D)** **Psoriasis** presents with well-circumscribed raised papules and plaques covered with a thick silvery scale. The lesions are located on the scalp, trunk, and extensor areas of the extremities (elbows and knees).

**(Choice E)** **Seborrheic keratoses** occur in elderly individuals and present with "stuck-on", deeply pigmented or flesh-colored lesions with a velvety or "greasy" surface.

### Educational objective:

Actinic keratosis (AK) develops on chronically sun-exposed areas of the skin in predisposed individuals. The lesions consist of erythematous papules with a central scale and a rough "sandpaper-like" texture. AKs are considered premalignant lesions and have the potential to progress to squamous cell carcinoma.





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pruritic erythematous papules and plaques. Light microscopy demonstrates spongiosis (edema of the

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pruritic erythematous papules and plaques. Light microscopy demonstrates spongiosis (edema of the

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Psoriasis Plaque psoriasis



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[Plaque psoriasis](#)



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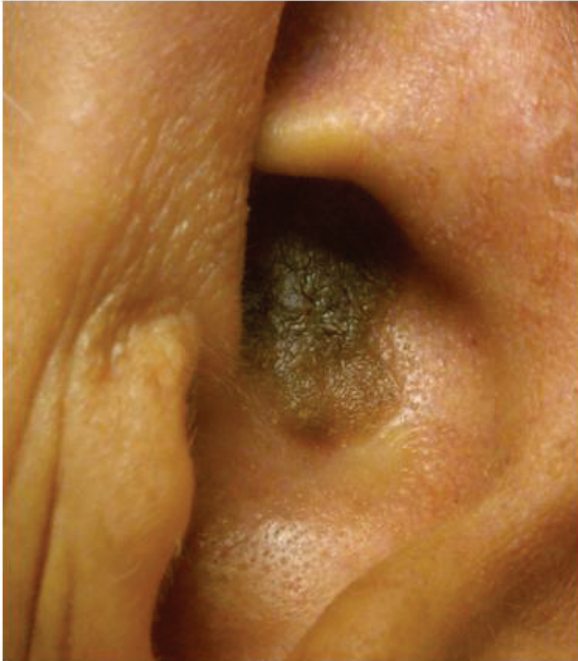
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pruritic erythematous papules and plaques. Light microscopy demonstrates spongiosis (edema of the

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Seborrheic Keratoses

Seborrheic keratosis, irritated



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pruritic erythematous papules and plaques. Light microscopy demonstrates spongiosis (edema of the

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Seborrheic Keratoses Seborrheic keratosis, irritated



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A 32-year-old woman is brought to the emergency department due to "bruising." She has a chronic mental disability and lives in a group home. Care staff members accompanying the patient report that she fell 3 days ago but has not mentioned any pain. No signs of injury were noted until a large area of discoloration was seen at the upper arm during bathing. Past medical history is unremarkable, and the patient takes no medications. Vital signs are normal. Skin examination findings are shown in the image below. There is no associated warmth, and the patient shows no signs of discomfort during palpation of the affected area.





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Which of the following terms best describes this abnormality?

- ☐ A. Angioma
- ☐ B. Ecchymosis
- ☐ C. Lentigo
- ☐ D. Petechia
- ☐ E. Purpura
- ☐ F. Telangiectasia

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Which of the following terms best describes this abnormality?

☐ A. Angioma (3%)

☒ B. Ecchymosis (80%)

☐ C. Lentigo (1%)

☐ D. Petechia (0%)

☐ E. Purpura (12%)

☐ F. Telangiectasia (1%)

Correct

80%

37 secs

02/07/2021

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This patient has a large area of **ecchymosis** involving the upper extremity. Patients and caregivers often use the term "bruise" to describe a variety of hemorrhagic skin lesions. However, the specific visual appearance often gives clues to the etiology of the lesion.

An ecchymosis is a cutaneous or subcutaneous collection of **extravasated blood** measuring at least 1 cm in diameter. Ecchymoses can arise superficially without a history of noticeable trauma, but they frequently indicate a deep hemorrhage (hematoma) due to bony fracture, ligamentous rupture, or muscular injury. These lesions do not blanch under pressure because the red blood cells are not contained within the vasculature. Ecchymoses often pass through an evolution of color change (blue or red to brown, green, and yellow), which can be used to estimate the age of the injury. This property is especially useful in cases of suspected abuse when other historical details are unknown or inconsistent.

**(Choice A)** Angiomas are chronic vascular malformations that most commonly appear as soft, well-demarcated, red or blue nodules. **Capillary hemangiomas** are usually small and superficial whereas cavernous hemangiomas are usually larger and more likely to involve deeper structures.

**(Choice C)** **Lentigines** are small tan or brown macules most often seen on the sun-exposed skin of a middle-aged or elderly person.

**(Choices D and E)** **Petechiae** (<5 mm diameter) and **purpura** (5 mm to 1 cm) are cutaneous or

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(Choices D and E) Petechiae (<5 mm diameter) and purpura (5 mm to 1 cm) are cutaneous or

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(Choices D and E) Petechiae (<5 mm diameter) and purpura (5 mm to 1 cm) are cutaneous or



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demarcated, red or blue nodules. **Capillary hemangiomas** are usually small and superficial whereas cavernous hemangiomas are usually larger and more likely to involve deeper structures.

**(Choice C)** **Lentigines** are small tan or brown macules most often seen on the sun-exposed skin of a middle-aged or elderly person.

**(Choices D and E)** **Petechiae** (<5 mm diameter) and **purpura** (5 mm to 1 cm) are cutaneous or subcutaneous collections of extravasated blood from small-vessel bleeding that are often associated with platelet dysfunction or capillary fragility. They occur most commonly in areas of increased venous pressure (eg, ankles, feet). Palpable purpura are an indicator of **leukocytoclastic vasculitis**.

**(Choice F)** **Telangiectasias** are small, permanent dilations of superficial capillaries or venules.

Telangiectasias will blanch under pressure and are commonly seen in aging, chronic solar damage, long-term glucocorticoid use, rosacea, and a variety of systemic disorders.

### Educational objective:

Ecchymoses frequently indicate a deep hemorrhage (hematoma) due to bony fracture, ligamentous rupture, or muscular injury. They do not blanch under pressure as the red blood cells are not contained within the vasculature. Ecchymoses often pass through an evolution of color change (blue or red to brown, green, and yellow), which can be used to estimate the age of the injury.



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demarcated, red or blue nodules. Capillary hemangiomas are usually small and superficial whereas

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demarcated, red or blue nodules. Capillary hemangiomas are usually small and superficial whereas

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A 55-year-old man comes to the emergency department with fever and chills. He has a history of acute myeloid leukemia for which he is receiving chemotherapy. His temperature is 38.3 C (101 F), blood pressure is 90/50 mm Hg, pulse is 124/min, and respirations are 22/min. Physical examination is notable for multiple skin patches with necrotic centers and occasional ulcerations, as shown in the image below.



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Laboratory results are as follows:

Complete blood count

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Laboratory results are as follows:

Complete blood count

Platelets

240,000/mm<sup>3</sup>

Leukocytes

800/mm<sup>3</sup>

Neutrophils

60%

Serum chemistry

Creatinine

0.9 mg/dL

Coagulation studies

Prothrombin time

12 sec

Activated partial thromboplastin time

33 sec

Blood cultures are drawn. Which of the following organisms is most likely responsible for this patient's

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Prothrombin time

12 sec

Activated partial thromboplastin time

33 sec

Blood cultures are drawn. Which of the following organisms is most likely responsible for this patient's symptoms?

☐ A. *Escherichia coli*

☐ B. *Haemophilus influenzae*

☐ C. *Klebsiella pneumoniae*

☐ D. *Pseudomonas aeruginosa*

☐ E. *Streptococcus pneumoniae*

☐ F. *Streptococcus pyogenes*

Submit

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Prothrombin time

12 sec

Activated partial thromboplastin time

33 sec

Blood cultures are drawn. Which of the following organisms is most likely responsible for this patient's symptoms?

A. *Escherichia coli* (4%)

B. *Haemophilus influenzae* (2%)

C. *Klebsiella pneumoniae* (4%)

D. *Pseudomonas aeruginosa* (54%)

E. *Streptococcus pneumoniae* (3%)

F. *Streptococcus pyogenes* (30%)

Correct

54%

01 min, 12 secs

02/27/2021

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This immunosuppressed patient has **febrile neutropenia** (absolute neutrophil count [ANC] of  $0.60 \times 800 = 480/\text{mm}^3$ , likely in the setting of chemotherapy) and sepsis. With neutropenia (typically ANC  $<500/\text{mm}^3$ ), there is increased susceptibility to infections with gram-negative organisms such as *Pseudomonas aeruginosa*. The dermatologic lesions in this patient are consistent with **ecthyma gangrenosum (EG)**, which is strongly associated with ***P aeruginosa* bacteremia**.

Perivascular bacterial invasion of arteries and veins in the dermis and subcutaneous tissue, with subsequent release of exotoxins destructive to human tissue, leads to characteristic **skin patches** exhibiting **necrosis and ulceration** as a result of insufficient blood flow. *P aeruginosa* virulence factors that may contribute to EG include exotoxin A (protein synthesis inhibition), elastase (degrades elastin - important for blood vessel destruction), phospholipase C (degrades cellular membranes), and pyocyanin (generates reactive oxygen species).

Although gram-negative sepsis is sometimes associated with disseminated intravascular coagulation (DIC) and resultant purpuric skin lesions, DIC is unlikely given the normal platelet count and coagulation times (prothrombin and activated thromboplastin times).

**(Choice A)** *Escherichia coli* is not associated with EG. *E coli* is the most common cause of gram-negative sepsis, usually following urinary tract infections. Thrombotic thrombocytopenic purpura, hemolytic uremic





(prothrombin and activated thromboplastin times).

**(Choice A)** *Escherichia coli* is not associated with EG. *E coli* is the most common cause of gram-negative sepsis, usually following urinary tract infections. Thrombotic thrombocytopenic purpura-hemolytic uremic syndrome, sometimes seen with Shiga toxin-producing *E coli*, is classically associated with renal failure and thrombocytopenia (not seen in this patient).

**(Choices B and E)** *Streptococcus pneumoniae* and *Haemophilus influenza* are typically associated with respiratory infections and can be isolated from blood, cerebrospinal fluid, or respiratory sources. They are not associated with EG.

**(Choice C)** *Klebsiella pneumoniae* infection is most commonly associated with necrotizing pneumonia in elderly or immunocompromised patients.

**(Choice F)** *Streptococcus pyogenes* (Group A *Streptococcus*) frequently causes cutaneous infections (eg, [impetigo](#), [erysipelas](#)) and necrotizing fasciitis, a rapidly progressive deep tissue infection that spreads contiguously along the muscle fascia. Necrotizing fasciitis initially appears as a single site of infection with erythema, edema, warmth, and pain out of proportion to physical findings. This progresses to purpuric discoloration, bullae formation, and sensory loss due to tissue necrosis.

**Educational objective:**



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Educational objective\*

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respiratory infections and can be isolated from blood, cerebrospinal fluid, or respiratory sources. They are not associated with EG.

**(Choice C)** *Klebsiella pneumoniae* infection is most commonly associated with necrotizing pneumonia in elderly or immunocompromised patients.

**(Choice F)** *Streptococcus pyogenes* (Group A *Streptococcus*) frequently causes cutaneous infections (eg, [impetigo](#), [erysipelas](#)) and necrotizing fasciitis, a rapidly progressive deep tissue infection that spreads contiguously along the muscle fascia. Necrotizing fasciitis initially appears as a single site of infection with erythema, edema, warmth, and pain out of proportion to physical findings. This progresses to purpuric discoloration, bullae formation, and sensory loss due to tissue necrosis.

### Educational objective:

Ecthyma gangrenosum is a cutaneous necrotic disease with a strong association with *Pseudomonas aeruginosa* bacteremia. It occurs from perivascular invasion and release of tissue-destructive exotoxins, causing vascular destruction and insufficient blood flow to patches of skin that become edematous and subsequently necrose. *Pseudomonas* infections are common in patients who are neutropenic, are hospitalized, have burns, or have indwelling catheters.

### References





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A 46-year-old man comes to the office with the skin lesions shown in the photograph below. The patient first noticed the lesions a week ago after he returned from a trip to Hawaii. He has not had any other significant rashes or skin lesions but does have a history of autoimmune thyroiditis.

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Which of the following would most likely be seen on histopathologic examination of this patient's lesions?

- ☐ A. Absence of melanocytes in the epidermis
- ☐ B. Linear pattern of melanocyte proliferation
- ☐ C. Melanosome aggregates within the cytoplasm of melanocytes
- ☐ D. Normal melanocytes with diminished pigment transfer to keratinocytes
- ☐ E. Poor melanin formation in melanocytes

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Which of the following would most likely be seen on histopathologic examination of this patient's lesions?

- ☒ A. Absence of melanocytes in the epidermis (54%)
- ☐ B. Linear pattern of melanocyte proliferation (0%)
- ☐ C. Melanosome aggregates within the cytoplasm of melanocytes (4%)
- ☐ D. Normal melanocytes with diminished pigment transfer to keratinocytes (24%)
- ☐ E. Poor melanin formation in melanocytes (16%)

Correct

54%  
Answered correctly

01 min, 14 secs  
Time Spent

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Last Updated

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## Vitiligo



Well-defined, variably sized patches of depigmentation

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This patient has **vitiligo**, which is characterized by flat, well-circumscribed patches of **depigmentation** of variable size due to the partial or complete loss of melanocytes. These lesions often manifest by the second or third decade of life and can be more obvious in individuals with darkly pigmented skin. Vitiligo

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This patient has **vitiligo**, which is characterized by flat, well-circumscribed patches of **depigmentation** of variable size due to the partial or complete loss of melanocytes. These lesions often manifest by the second or third decade of life and can be more obvious in individuals with darkly pigmented skin. Vitiligo classically erupts on the face, extremities, axillae, groin, and over hard bony surfaces (eg, knees). Histologic examination of the affected epidermis would demonstrate the **absence of melanocytes** and melanin pigment.

The pathogenesis of melanocyte loss in vitiligo is likely a combination of **autoimmune activity**, neurohumoral toxicity specific for melanocytes, and melanocytic self-destruction (eg, toxic intermediate exposure during melanin synthesis). Autoimmune activity seems to have the strongest correlation with vitiligo due to the presence of circulating melanocyte antibodies in patients and the high prevalence of concurrent autoimmune disorders (e.g., type I diabetes mellitus, pernicious anemia, Addison disease, autoimmune thyroiditis).

**(Choice B)** Lentigines are small, benign pigmented lesions characterized by linear melanocytic hyperplasia.

**(Choice C)** Café-au-lait spots demonstrate increased melanosome aggregates within the melanocyte

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concurrent autoimmune disorders (e.g., type I diabetes mellitus, pernicious anemia, Addison disease, autoimmune thyroiditis).

**(Choice B)** Lentigines are small, benign pigmented lesions characterized by linear melanocytic hyperplasia.

**(Choice C)** Café-au-lait spots demonstrate increased melanosome aggregates within the melanocyte cytoplasm. These macules are hyperpigmented and associated with neurofibromatosis type 1.

**(Choice D)** Postinflammatory hypopigmentation can occur after significant inflammatory skin lesions (eg, discoid lupus, psoriasis) and is characterized by redistribution of existing melanin within the skin and/or reduced transfer of melanin to keratinocytes.

**(Choice E)** Individuals with albinism have melanocytes that do not produce melanin because of absent or defective tyrosinase.

**Educational objective:**

Vitiligo is a common condition characterized by the loss of epidermal melanocytes. It occurs more commonly in patients with autoimmune disorders (eg, autoimmune thyroiditis, type I diabetes) and results in well-defined, variably sized patches of hypopigmentation.



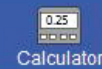
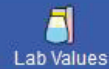


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A 48-year-old woman comes to the office 10 days after undergoing breast reduction surgery. She feels well overall and is taking acetaminophen as needed for pain control. Vital signs are normal. Examination of the breasts reveals intact surgical incisions without drainage; the incisions are pink, shiny, and slightly warm. The surrounding skin has mild edema but no erythema. Which of the following wound healing processes is most likely occurring at this time?

- ☐ A. Degranulation of mast cells
- ☐ B. Extensive crosslinking of collagen
- ☐ C. Infiltration of polymorphonuclear leukocytes
- ☐ D. Proliferation of vascular endothelial cells
- ☐ E. Synthesis of type II collagen

Submit



A 48-year-old woman comes to the office 10 days after undergoing breast reduction surgery. She feels well overall and is taking acetaminophen as needed for pain control. Vital signs are normal. Examination of the breasts reveals intact surgical incisions without drainage; the incisions are pink, shiny, and slightly warm. The surrounding skin has mild edema but no erythema. Which of the following wound healing processes is most likely occurring at this time?

- ☐ A. Degranulation of mast cells (2%)
- ☐ B. Extensive crosslinking of collagen (19%)
- ☐ C. Infiltration of polymorphonuclear leukocytes (8%)
- ☒ D. Proliferation of vascular endothelial cells (62%)
- ☐ E. Synthesis of type II collagen (6%)

Correct

Collecting Statistics



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Time Spent

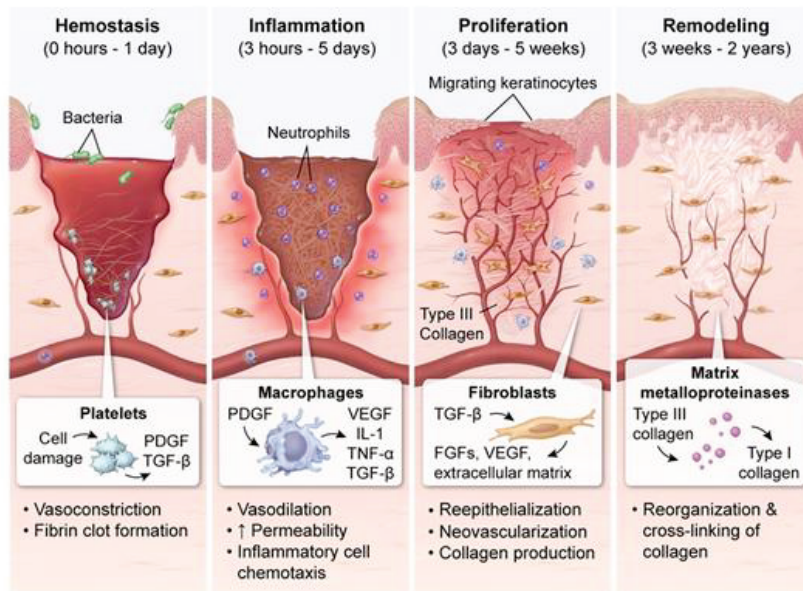


03/12/2021  
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## Exhibit Display

## Phases of wound healing



FGF = fibroblast growth factor; PDGF = platelet-derived growth factor;  
TGF- $\beta$  = transforming growth factor-beta; VEGF = vascular endothelial growth factor.

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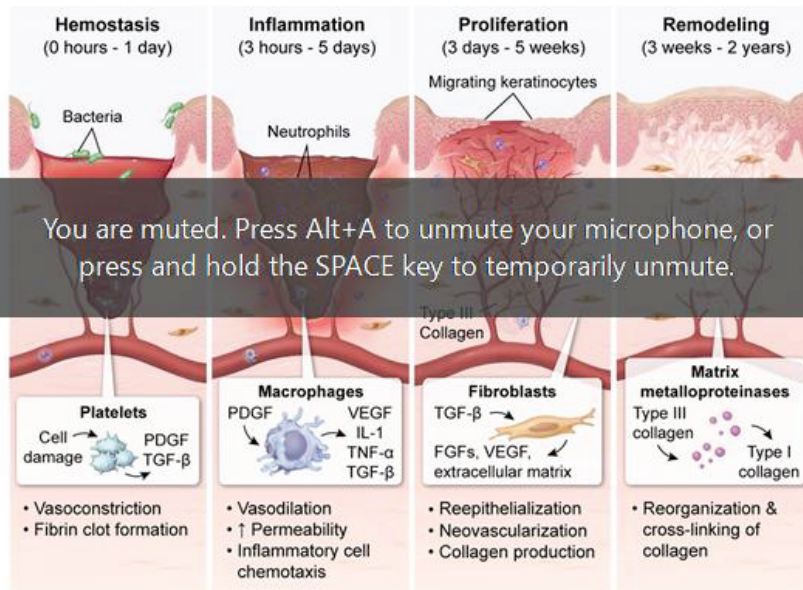
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## Exhibit Display

## Phases of wound healing



FGF = fibroblast growth factor; PDGF = platelet-derived growth factor;  
TGF- $\beta$  = transforming growth factor-beta; VEGF = vascular endothelial growth factor.

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FGF = fibroblast growth factor; PDGF = platelet-derived growth factor;  
TGF- $\beta$  = transforming growth factor-beta; VEGF = vascular endothelial growth factor.

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Ten days after surgery, this patient's intact, healing surgical incisions are most likely undergoing a type of neovascularization called **angiogenesis**, the process by which **new blood vessels** sprout and grow into the wound from surrounding, uninjured vessels.

Angiogenesis primarily occurs during the **proliferation phase** of wound healing, which begins around day 3 (overlapping with the end of the inflammatory phase) and lasts approximately 5 weeks. During the proliferation phase, fibroblasts multiply and synthesize ground substance and type III collagen, which form an amorphous gel into which new capillaries can grow. In addition, fibroblasts secrete **fibroblast growth factor** and **vascular endothelial growth factor**, which stimulate endothelial cell proliferation, migration, and differentiation—leading to the formation of new capillaries.

By increasing the number of capillaries within the healing surgical incision, angiogenesis increases blood flow to the area, causing the **pink and slightly warm** characteristics of the wound at this stage. The incision's newly formed epithelium (ie, reepithelialization) typically has a shiny appearance as well.

**(Choices A and C)** Degranulation of mast cells and infiltration of polymorphonuclear leukocytes occur during the inflammation phase, which starts within hours of the injury and lasts approximately 5 days. During this phase, there is often moderate edema, redness, and/or warmth of the wound and nearby soft

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**(Choice E)** Collagen synthesis begins during the proliferation phase, along with angiogenesis. However, fibroblasts predominantly synthesize type III collagen; type III collagen is then replaced with type I collagen during the maturation phase. **Type II collagen** is primarily found in articular and hyaline cartilage rather than the skin.

Angiogenesis is the process by which new blood vessels are formed. It primarily occurs during the proliferation phase of wound healing and is stimulated by growth factors such as fibroblast growth factor and vascular endothelial growth factor.

- Angiogenesis.



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During this phase, tissues due to high is 10 days out from

**(Choice B)** Extens during the final pha years (not 10 days

**(Choice E)** Collag fibroblasts predomi during the maturati than the skin.

**Educational objec**

Angiogenesis is the proliferation phase and vascular endot

**References**

- Angiogenesis.

Collagen subtypes

Type	Locations	Associated diseases
I	Skin, bone, tendons, ligaments, dentin, cornea, blood vessels & scar tissue	Osteogenesis imperfecta
II	Cartilage, vitreous humor & nucleus pulposus	Skeletal dysplasias
III	Skin, lungs, intestines, blood vessels, bone marrow, lymphatics & granulation tissue	Vascular Ehlers-Danlos syndrome (Type IV)
IV	Basement membrane	Alport syndrome

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A 28-year-old man comes to the office due to a rash on the lower extremity. The patient noticed a pruritic papule on the dorsum of his right foot just prior to returning from a south Florida beach 2 days ago. He walked barefoot on the beach but does not recall any trauma. Since his return home, the rash and itching have progressively worsened. The patient has no other medical problems and takes no medications. Physical examination findings are shown below.



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Which of the following is the most likely cause of this patient's current condition?

☐ A. Brown recluse spider bite

☐ B. Hookworm infection

☐ C. *Mycobacterium marinum* infection

☐ D. *Sporothrix schenckii* infection

☐ E. *Staphylococcus aureus* infection

☐ F. *Vibrio vulnificus* infection

Submit

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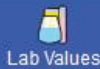
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Full Screen



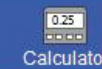
Tutorial



Lab Values



Notes



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Which of the following is the most likely cause of this patient's current condition?

- ☐ A. Brown recluse spider bite (2%)
- ☒ B. Hookworm infection (72%)
- ☐ C. *Mycobacterium marinum* infection (7%)
- ☐ D. *Sporothrix schenckii* infection (5%)
- ☐ E. *Staphylococcus aureus* infection (1%)
- ☐ F. *Vibrio vulnificus* infection (10%)

Correct



72%

Answered correctly



55 secs

Time spent



10/21/2020

Last updated

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This patient, who developed a serpiginous, pruritic rash shortly after walking barefoot on a beach, likely has **hookworm infection**. Hookworms spread when **egg-containing feces** are deposited into shady, warm, moist sand or soil. Eggs hatch into larvae and are transmitted when they come into **direct contact with human skin** (eg, when walking barefoot).

Dermal penetration is usually marked by a **pruritic maculopapular lesion** ("ground itch") at the site of larval entry (eg, foot, toe webs). Spread of larvae through the adjacent dermal tissue can lead to the formation of migrating, reddish-brown, **serpiginous tracks**. Deeper spread may occur, depending on the species of infecting hookworm, as follows:

- **Human hookworms** (eg, *Necator americanus*, *A duodenale*) penetrate the basement membrane and spread from the dermis to the bloodstream. They rupture into the alveoli and are coughed up and swallowed into the small intestine. There, larvae mature into adult hookworms that feed on blood from the duodenal mucosa (often causing iron deficiency anemia) and shed up to 10,000 eggs/day, thereby spreading the infection to others.
- Cat and dog hookworms (eg, *Ancylostoma braziliense*, *A caninum*) cause a dermal eruption in humans but are unable to penetrate the cutaneous basement membrane and spread to deeper tissues.

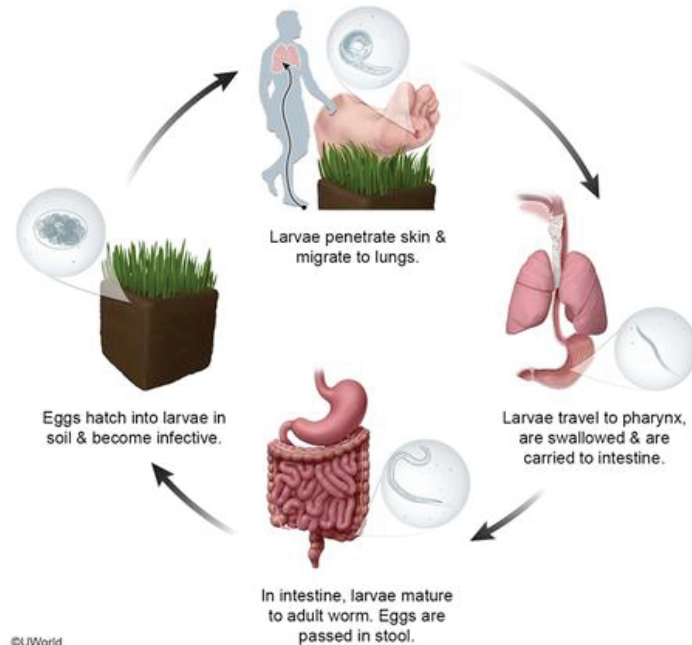
Therefore, larvae do not mature into adult hookworms or spread from human-to-human (humans are





### Exhibit Display

#### Human hookworm life cycle



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Therefore, larvae do not mature into adult hookworms or spread from human-to-human (humans are



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- Cat and dog hookworms (eg, *Ancylostoma braziliense*, *A. caninum*) cause a dermal eruption in humans but are unable to penetrate the cutaneous basement membrane and spread to deeper tissues. Therefore, larvae do not mature into adult hookworms or spread from human-to-human (humans are incidental hosts).

**(Choice A)** A brown recluse spider bite usually appears as a red plaque or papule with central pallor; it may develop a dark central eschar that ulcerates due to necrosis. Pain is often severe.

**(Choice C)** *Mycobacterium marinum* lesions usually form a few weeks after exposure to contaminated fresh/salt water (eg, swimming pool, fish tank). Lesions begin as solitary papules or nodules that eventually ulcerate and scar. Serpiginous tracts would be uncommon.

**(Choice D)** *Sporothrix schenckii*, a dimorphic fungus, is usually transmitted when contaminated organic material (eg, moss, soil) is inoculated into the skin or subcutaneous tissue. A papule forms at the inoculation site and usually ulcerates; additional lesions form along the proximal route of lymphatic drainage.

**(Choice E)** *Staphylococcus aureus* is the most common cause of purulent cellulitis. Lesions tend to develop over days and are characterized by painful areas of fluctuance with surrounding erythema.

**(Choice F)** *Vibrio vulnificus* is a free-living bacterium that grows in brackish water and marine





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(Choice D) *Sporothrix schenckii*, a dimorphic fungus, is usually transmitted when contaminated organic

material (eg, moss, soil) is inoculated into the skin or subcutaneous tissue. A papule forms at the inoculation site and usually ulcerates; additional lesions form along the proximal route of lymphatic drainage.

(Choice E) *Staphylococcus aureus* is the most common cause of purulent cellulitis. Lesions tend to develop over days and are characterized by painful areas of fluctuance with surrounding erythema.

(Choice F) *Vibrio vulnificus* is a free-living bacterium that grows in brackish water and marine environments. It can contaminate wounds and cause mild cellulitis. More severe manifestations (eg, myositis, necrotizing fasciitis, sepsis) can develop in patients with certain underlying comorbidities (eg, liver disease, hemochromatosis).

### Educational objective:

Hookworm infections are transmitted via direct contact between human skin and contaminated soil/sand (eg, walking barefoot). Dermal penetration is often characterized by an intensely pruritic papule that may form serpiginous tracks due to the subcutaneous migration of hookworm larvae.

Microbiology

Dermatology

Cutaneous larva migrans

Subject

System

Topic





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A 14-year-old girl is brought to the office for evaluation of a bump on her chest just below the right breast. The bump has been there for as long as she can remember, but it became a little larger 2-3 years ago. The bump also becomes tender just before she starts her menses. Menarche was at age 12. Her menses occur every 28 days and last 4-5 days. Examination shows Tanner stage 5 breasts. Both breasts and axillae appear normal. There is a soft, raised, hyperpigmented, 0.5-cm nontender lesion inferior to the right breast. Which of the following is the cause of this patient's presentation?

- ☐ A. Clonal proliferation of benign melanocytes (13%)
- ☐ B. Excessive sunlight exposure (0%)
- ☒ C. Failed involution of the mammary ridge (68%)
- ☐ D. Fat cells in a fibrous capsule (13%)
- ☐ E. Pedunculated outgrowth of normal skin (3%)

Correct

68%  
Answered correctly

53 secs  
Time Spent

12/25/2020  
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Mammary line

The diagram shows a female figure from the waist up, with arms raised. A red line, labeled 'Mammary line', runs vertically from the upper chest down to the pubic area. To the right of the chest, a bracket indicates the 'Position of accessory nipples' with four red dots. The main label 'Mammary line' is at the top left of the diagram.

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The most common congenital breast anomalies in women and men are **accessory nipples** (ie, **polythelia**, **supernumerary nipple**). They are due to **failure of involution of the mammary ridge**. Accessory nipples are usually **asymptomatic**. However, they **may swell or become tender** similar to normal breast tissue before or during menses, pregnancy, and lactation. They can occur anywhere along the embryonic milk line between the axilla and perineum and are bilateral in 50% of patients. Treatment is normally not needed. Histologically, the accessory nipple is identical to a normal nipple. Findings include **hyperpigmentation**, **epidermal thickening**, pilosebaceous structure of Montgomery areolar tubercles, smooth muscle bundles (areola), and possible mammary glands and multiple ducts.


**(Choice A)** **Congenital melanocytic nevi** are caused by the clonal proliferation of benign melanocytes in utero. They can be raised and are hyperpigmented.


**(Choice B)** Ephelides (eg, freckles) and **solar lentigines** are found on sun-exposed areas. Ephelides are caused by increased melanin production by melanocytes, whereas solar lentigo represents an increased proliferation of melanocytes themselves. They are both hyperpigmented and flat, but solar lentigines are often larger and occur in adults.

**(Choice D)** **Lipomas** are benign fatty tumors contained within a fibrous capsule. They present as a flesh-

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often larger and occur in adults.

**(Choice D)** [Lipomas](#) are benign fatty tumors contained within a fibrous capsule. They present as a flesh-colored, soft, and painless subcutaneous mass.

**(Choice E)** [Acrochorda](#), or skin tags, are benign and often pedunculated outgrowths of normal skin. They often develop in locations that experience frequent friction, such as beneath breast tissue or the axillae.

**Educational objective:**

Accessory nipples are the most common congenital breast anomaly resulting from failed regression of the mammary ridge in utero. They are usually asymptomatic but can become tender along with breast tissue during times of hormonal fluctuation.

**References**

- [Supernumerary nipples: an overview.](#)

Pathophysiology

Dermatology

Accessory nipple

Subject

System

Topic

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www.ncbi.nlm.nih.gov/pubmed/12769398



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A 34-year-old man comes to the office due to a persistent skin rash. He has a 6-month history of a scaly rash involving the upper and lower extremities that is associated with mild pruritus. The patient has attempted treatment with topical antihistamines and emollients without relief. Medical history is notable for childhood asthma and orolabial herpes simplex virus infection. He does not use tobacco or alcohol and works as a sales associate for a home improvement store. On examination, the patient has skin lesions as shown in the image below.



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This patient's disorder is most likely associated with which of the following extradermal complications?

- ☐ A. Chronic glomerulonephritis
- ☐ B. Deforming joint disease
- ☐ C. Medullary thyroid cancer
- ☐ D. Peripheral neuropathy
- ☐ E. Pulmonary fibrosis

Submit





This patient's disorder is most likely associated with which of the following extradermal complications?

- ☐ A. Chronic glomerulonephritis (6%)
- ☒ B. Deforming joint disease (81%)
- ☐ C. Medullary thyroid cancer (1%)
- ☐ D. Peripheral neuropathy (4%)
- ☐ E. Pulmonary fibrosis (5%)

Correct

81%

01 min, 59 secs

01/30/2021



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This patient with well-demarcated, scaly, erythematous plaques involving extensor surfaces of the extremities has typical features of **psoriasis**. Patients with psoriasis frequently develop additional complications, including:

- Psoriatic arthritis
- Nail changes: yellow-brown discoloration, **pitting**, thickening, or crumbling
- Inflammatory disorders of the eye: conjunctivitis, blepharitis, or **uveitis**

**Psoriatic arthritis** is an inflammatory disorder affecting the synovium and often the insertion of tendons and ligaments (ie, enthesopathy). It typically manifest as asymmetric oligoarthritis or symmetric **polyarthritis** (resembling rheumatoid arthritis) that often affects the distal interphalangeal joints. In severe cases, patients can develop an aggressive and destructive **arthritis mutilans**. The risk is increased in patients who are human leukocyte antigen B27–positive.


**(Choice A)** Chronic glomerulonephritis frequently occurs in systemic lupus erythematosus. However, lupus is typically associated with an erythematous **malar rash**.


**(Choice C)** Medullary thyroid cancer is frequently linked to multiple endocrine neoplasia type 2.

**(Choice D)** Skin lesions, renal insufficiency, and peripheral neuropathy (eg, mononeuropathy multiplex)




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(Choice A)

Chronic glomerulonephritis frequently occurs in systemic lupus erythematosus. However, lupus is typically associated with an erythematous malar rash.

(Choice C)

Medullary thyroid cancer is frequently linked to multiple endocrine neoplasia type 2.

(Choice D)

Skin lesions, renal insufficiency, and peripheral neuropathy (eg, mononeuropathy multiplex) are frequent findings in polyarteritis nodosa, a vasculitis affecting medium-sized arteries.

(Choice E)

Pulmonary fibrosis is a common extradermal manifestation of systemic sclerosis (scleroderma).

Educational objective:

Common complications of psoriasis include psoriatic arthritis, nail changes, and uveitis.

References

Clinical features and diagnostic considerations in psoriatic arthritis.

Pathology

Subject

Dermatology

System

Psoriasis

Topic

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An 8-year-old Middle Eastern immigrant is brought to the physician by his parents for a low-grade fever and skin rash. The child's mother says that the rash started on his face and spread rapidly down his body. The boy recently returned from a month-long trip to Yemen, where he visited relatives. Physical examination shows a generalized, fine, pinkish maculopapular rash and tender lymphadenopathy bilaterally behind the ears. Which of the following is the most likely cause of this patient's disease?

- ☐ A. Herpesvirus
- ☐ B. Togavirus
- ☐ C. Reovirus
- ☐ D. Paramyxovirus
- ☐ E. Parvovirus

Submit



An 8-year-old Middle Eastern immigrant is brought to the physician by his parents for a low-grade fever and skin rash. The child's mother says that the rash started on his face and spread rapidly down his body. The boy recently returned from a month-long trip to Yemen, where he visited relatives. Physical examination shows a generalized, fine, pinkish maculopapular rash and tender lymphadenopathy bilaterally behind the ears. Which of the following is the most likely cause of this patient's disease?

- ☐ A. Herpesvirus (3%)
- ✓ ☐ B. Togavirus (51%)
- ☐ C. Reovirus (2%)
- ✗ ☒ D. Paramyxovirus (31%)
- ☐ E. Parvovirus (10%)

**Incorrect**

Correct answer

B



51%

Answered correctly



02 mins, 51 secs

Time Spent



11/22/2020

Last Updated



Many immigrants to the United States will not have completed the vaccination regimen recommended by the Centers for Disease Control and Prevention. It is likely that this patient was not vaccinated against measles, mumps, and rubella (MMR) at age 12-15 months. Among the acute viral exanthems, measles (rubeola) and German measles (rubella) are characterized by a maculopapular rash that begins on the face and spreads to the trunk and extremities. Compared to rubeola, the rash of rubella typically spreads faster and does not darken or coalesce. Postauricular and occipital lymphadenopathy is particularly common in rubella, which is caused by a togavirus.

**(Choice A)** Varicella zoster virus tends to produce a maculopapular rash that begins on the trunk and spreads centrifugally to involve the face and extremities. Roseola (HHV-6) causes exanthem subitum (also called roseola infantum), which is characterized by a transient maculopapular rash that appears for a few days on the chest and trunk once the patient's fever subsides.

**(Choice C)** A coltivirus in the Reoviridae family is responsible for Colorado tick fever. This infection occurs primarily in the Rocky Mountain states and is characterized by fever, vomiting, myalgias, and weakness. A maculopapular rash is not typically seen.

**(Choice D)** Among the paramyxoviruses of medical importance, only measles (rubeola) typically produces



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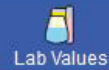
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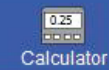
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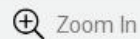


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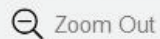


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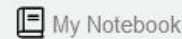
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primarily in the Rocky Mountain states and is characterized by fever, vomiting, myalgias, and weakness. A maculopapular rash is not typically seen.

**(Choice D)** Among the paramyxoviruses of medical importance, only measles (rubeola) typically produces a rash. Rubella is more often associated with postauricular lymphadenopathy and tenderness than is rubeola.

**(Choice E)** A parvovirus is responsible for fifth disease (erythema infectiosum). This illness is first characterized by redness of the cheeks ("slapped-cheek" appearance), followed by a maculopapular rash on the extremities and trunk. Postauricular tenderness is not a common manifestation.

**Educational objective:**

In a susceptible child, a febrile maculopapular rash that begins on the face and spreads to the trunk and extremities is suggestive of rubeola (measles) or rubella (German measles). The additional finding of postauricular lymphadenopathy indicates that rubella is the most likely etiology.

Microbiology  
Subject

Dermatology  
System

Rubella  
Topic

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A 64-year-old man comes to the physician with several lesions on his forehead. The patient has been a gardener for much of his life. The photograph below shows findings from the physical examination.





Mark



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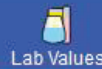
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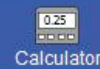
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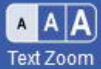
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On palpation, the lesions have a rough grainy texture. Biopsy reveals atypical keratinocytes with hyperkeratosis and parakeratosis. This patient's lesions put him at greatest risk for developing which of the following conditions?

- ☐ A. Basal cell carcinoma
- ☐ B. Dermatofibroma
- ☐ C. Kaposi sarcoma
- ☐ D. Melanoma
- ☐ E. Psoriasis
- ☐ F. Squamous cell carcinoma

**Submit**

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Feedback



Suspend



End Block



Mark



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Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



On palpation, the lesions have a rough grainy texture. Biopsy reveals atypical keratinocytes with hyperkeratosis and parakeratosis. This patient's lesions put him at greatest risk for developing which of the following conditions?

- ☐ A. Basal cell carcinoma (14%)
- ☐ B. Dermatofibroma (0%)
- ☐ C. Kaposi sarcoma (0%)
- ☐ D. Melanoma (2%)
- ☐ E. Psoriasis (6%)
- ☒ F. Squamous cell carcinoma (75%)







Mark



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Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient's forehead lesions are characteristic of **actinic keratoses (AKs)**, which are small, scaly, erythematous lesions with a sandpaper texture occurring on sun-exposed areas. On light microscopy, AKs show **hyperkeratosis** (hyperplasia of the stratum corneum), **parakeratosis** (retention of nuclei in the stratum corneum), and **atypical keratinocytes** with pleomorphic nuclei and multiple mitoses. There may also be pigment irregularities and dilated blood vessels affecting the surrounding skin, which are consistent with chronic sun exposure.

AKs do not invade the dermis and are considered to be **premalignant lesions**. Over several years, a small percentage of AKs **transform** into invasive **squamous cell carcinoma (SCC)**, a change reflected by an increase in lesion size and thickness, dermal invasion, and metastatic potential.

**(Choice A)** Basal cell carcinoma (BCC) is the most common skin cancer. It arises on sun-exposed areas and has a very low tendency to metastasize (in contrast to melanoma). BCC often presents as pearly papules with central depression or ulceration. Histologically, BCC features nests of basaloid cells and peripheral palisading of nuclei. It is far more likely for AK to progress to SCC than to BCC.

**(Choice B)** Dermatofibromas (superficial benign fibrous histiocytomas) result from the benign proliferation of fibroblasts. They commonly arise on the lower extremities as solitary nodules.



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Previous



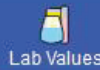
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Full Screen



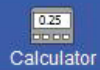
Tutorial



Lab Values



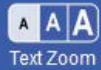
Notes



Calculator



Reverse Color

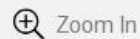


Text Zoom

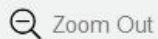


Settings

## Exhibit Display

Basal cell carcinoma, ulcerated Basal cell carcinoma, ulcerated

Zoom In



Zoom Out



Reset



New | Existing



My Notebook



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Feedback



Suspend



End Block

## Exhibit Display

Basal cell carcinoma, ulcerated [Basal cell carcinoma, ulcerated](#)

Zoom In

Zoom Out

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Item 16 of 40

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Tutorial



Lab Values



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Calculator



Reverse Color

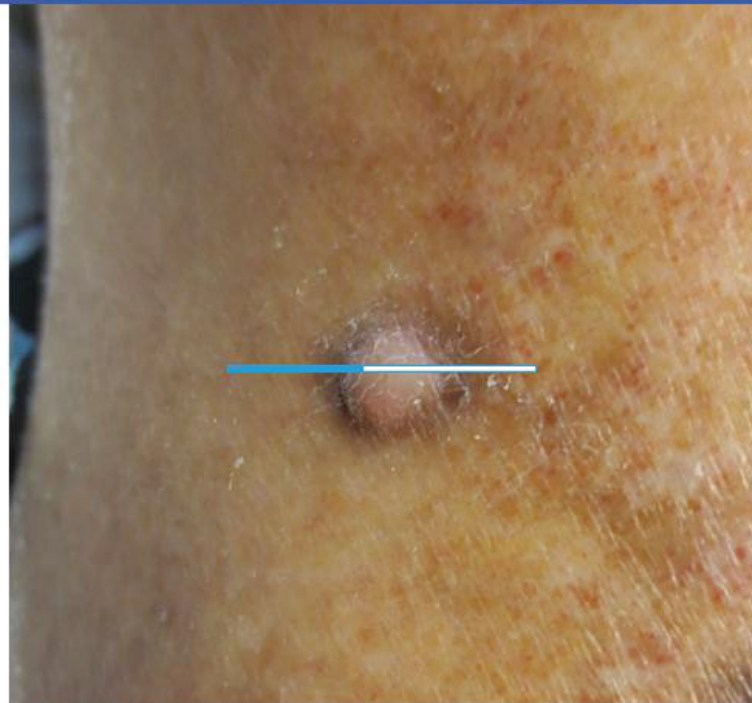


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### Exhibit Display



Zoom In

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Feedback

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End Block



**(Choice B)** **Dermatofibromas** (superficial benign fibrous histiocytomas) result from the benign proliferation of fibroblasts. They commonly arise on the lower extremities as solitary nodules.

**(Choice C)** **Kaposi sarcoma** is associated with human herpesvirus-8 (HHV-8) and classically occurs in patients with HIV. Lesions typically appear as palpable macules, plaques, and nodules that are usually a dark brown to violet color.

**(Choice D)** **Melanoma** is a cancer arising from the malignant transformation of melanocytes. Lesions have irregular borders and marked color variegation. AK is not a precursor to melanoma.

**(Choice E)** **Psoriasis** commonly presents as hyperkeratotic plaques that affect the scalp, knees, and elbows. It is characterized histologically by clubbed rete ridges, hyperkeratosis, neutrophils in the stratum corneum, and perivascular lymphocytic infiltrates.

**Educational objective:**

Actinic keratoses (AKs) are small (usually <1 cm), erythematous epidermal lesions with adherent scale that are the result of chronic sun exposure. Histologic findings include keratinocyte atypia, hyperkeratosis, and parakeratosis. A small percentage of AKs progress to invasive squamous cell carcinoma; therefore, frequent monitoring is necessary.





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Previous



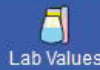
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Full Screen



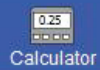
Tutorial



Lab Values



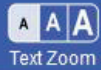
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Calculator



Reverse Color



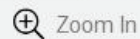
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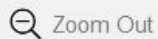
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## Exhibit Display

Kaposi sarcoma Kaposi sarcoma, HIV/AIDS-associated form



Zoom In



Zoom Out



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New | Existing



My Notebook



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Feedback



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End Block





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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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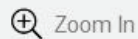


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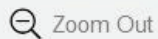


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## Exhibit Display

Kaposi sarcoma [Kaposi sarcoma, HIV/AIDS-associated form](#)

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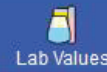
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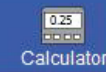
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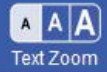
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Settings

## Exhibit Display

Malignant melanoma Melanoma

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End Block

## Exhibit Display

Malignant melanoma [Melanoma](#)

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Settings

### Exhibit Display



Zoom In

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End Block



A 62-year-old man comes to the office due to an intensely pruritic facial rash for the past 3 days. The patient uses no facial cosmetic products but has frequently dyed his hair during the past year; he last dyed his hair 5 days ago and also recalls developing a similar rash the previous time he used hair dye. The patient has a history of asthma, hypertension, and diabetes mellitus. He does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. Physical examination findings are shown in the exhibit.

Which of the following are primarily involved in the pathogenesis of this patient's rash?

- ☐ A. CD8<sup>+</sup> T cells and interferon gamma
- ☐ B. Mast cells and histamine
- ☐ C. Neutrophils and myeloperoxidase
- ☐ D. Plasma cells and immunoglobulins
- ☐ E. Regulatory T cells and interleukin-10

Submit





Item 15 of 40

Question Id: 20556



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Tutorial



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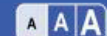
Notes



Calculator



Reverse Color



Text Zoom



Settings

### Exhibit Display



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Zoom In



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Feedback



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End Block





A 62-year-old man comes to the office due to an intensely pruritic facial rash for the past 3 days. The patient uses no facial cosmetic products but has frequently dyed his hair during the past year; he last dyed his hair 5 days ago and also recalls developing a similar rash the previous time he used hair dye. The patient has a history of asthma, hypertension, and diabetes mellitus. He does not use tobacco, alcohol, or illicit drugs. Vital signs are within normal limits. Physical examination findings are shown in the exhibit.

Which of the following are primarily involved in the pathogenesis of this patient's rash?

- ☒ A. CD8<sup>+</sup> T cells and interferon gamma (49%)
- ☐ B. Mast cells and histamine (37%)
- ☐ C. Neutrophils and myeloperoxidase (2%)
- ☐ D. Plasma cells and immunoglobulins (5%)
- ☐ E. Regulatory T cells and interleukin-10 (5%)

Correct



49%

Answered correctly



01 min, 35 secs

Time Spent



02/15/2021

Last Updated

Block Time Remaining: 00:47:53

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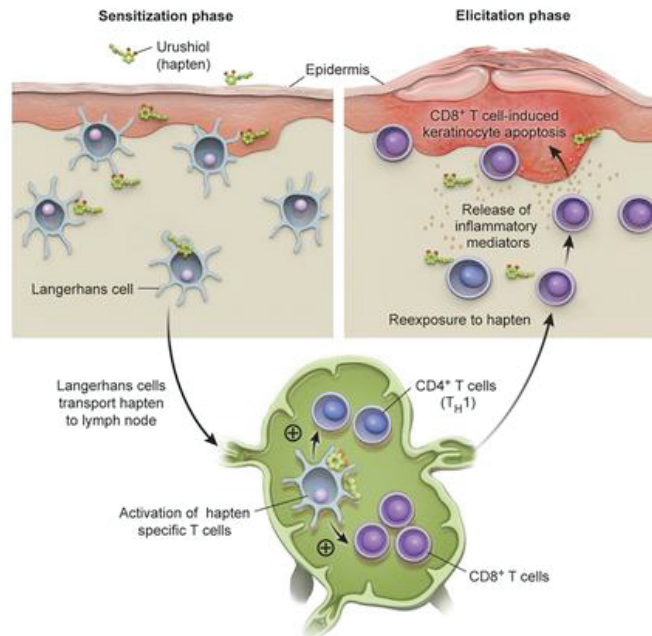
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End Block

## Exhibit Display

## Urushiol-induced contact dermatitis



Zoom In

Zoom Out

Reset

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My Notebook



This patient developed erythema and pruritus on the scalp, face, and neck 2 days after reexposure to hair dye. Hair products, including dye, frequently contain allergenic molecules (eg, p-phenylenediamine) that can cause **allergic contact dermatitis** (ACD). ACD is a type IV (**delayed-type**) hypersensitivity reaction that occurs in 2 phases:

1. **Sensitization:** Cutaneous **Langerhans cells** take up haptens (small molecules that bind to proteins and alter their immune appearance) and present hapten-peptide complexes to naive CD4<sup>+</sup> and CD8<sup>+</sup> T cells in regional lymph nodes, resulting in clonal expansion of hapten-sensitive T cells. This phase takes **10-14 days** and does not result in cutaneous lesions.
2. **Elicitation:** On reexposure to the hapten, sensitized T cells are recruited to skin for activation by hapten-protein conjugates displayed on cutaneous antigen-presenting cells. Activated **CD8<sup>+</sup> T cells**, the main effector cells in ACD, release cytotoxins (eg, perforin, granzymes) and express Fas ligand to induce keratinocyte apoptosis. They also amplify the inflammatory response by releasing cytokines (eg, **interferon gamma**) and recruiting additional inflammatory cells (eg, macrophages). This phase occurs **2-3 days** following reexposure to the hapten and results in erythema, pruritus, and vesicles.

**(Choice B)** Mast cells are primarily responsible for immediate (type I) hypersensitivity reactions. On reexposure, allergens bind to allergen-specific IgEs on mast cells, causing immediate degranulation and







occurs **2-3 days** following reexposure to the hapten and results in erythema, pruritus, and vesicles.

**(Choice B)** Mast cells are primarily responsible for immediate (type I) hypersensitivity reactions. On reexposure, allergens bind to allergen-specific IgEs on mast cells, causing immediate degranulation and release of vasoactive peptides (eg, histamine), resulting in **urticaria** and, when severe, anaphylaxis. Onset is rapid (minutes), unlike this patient's delayed (48-hr) response. Furthermore, individual wheals of urticaria resolve within 24 hours, rather than days.

**(Choice C)** Neutrophils phagocytose bacteria and fungi and kill them by generating reactive oxygen species (NADPH oxidase) and hypochlorous acid (myeloperoxidase). Although neutrophils play a role in defense against cutaneous infections (eg, cellulitis, which is painful rather than pruritic), this patient's rash is more consistent with contact dermatitis.

**(Choice D)** Immunoglobulins produced by plasma cells are responsible for **type II and III** hypersensitivity reactions. ACD does not involve plasma cells or antibodies.

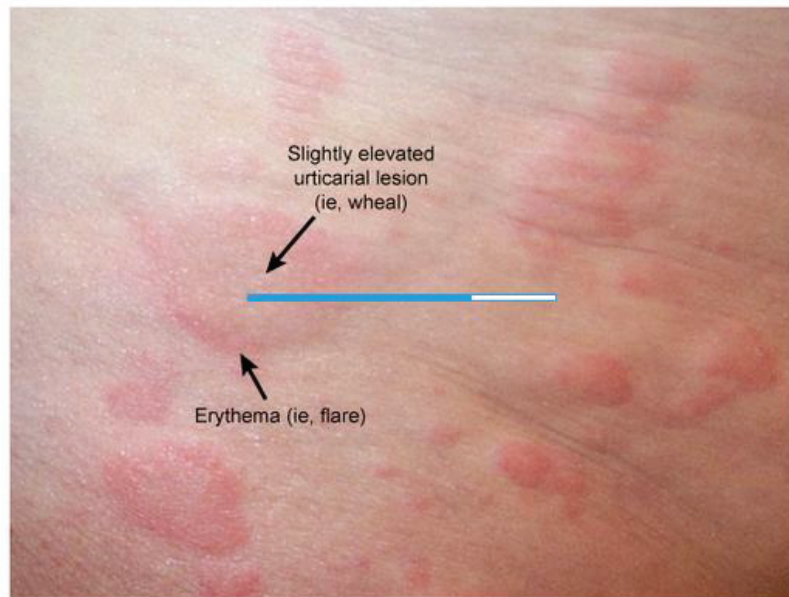
**(Choice E)** Regulatory T cells are CD4<sup>+</sup> lymphocytes that play an inhibitory role in the immune response. They secrete cytokines (eg, interleukin-10) that inhibit macrophage function and antagonize proinflammatory cytokines (eg, interferon gamma). This anti-inflammatory effect is important in suppressing autoimmune diseases.



occurs 2-3 days following reexposure to the hapten and results in erythema, pruritus, and vesicles

## Exhibit Display

## Wheal and flare



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Zoom In

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My Notebook



occurs 2-3 day

## Exhibit Display

**(Choice B)** Mast c

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resolve within 24 h

**(Choice C)** Neutro

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**(Choice D)** Immur

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**(Choice E)** Regula

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Hypersensitivity reactions		
	Immunology	Examples
<b>Type I</b> (immediate)	IgE-mediated	<ul style="list-style-type: none"><li>• Anaphylaxis</li><li>• Urticaria</li></ul>
<b>Type II</b> (cytotoxic)	IgG & IgM autoantibody-mediated	<ul style="list-style-type: none"><li>• Autoimmune hemolytic anemia</li><li>• Goodpasture syndrome</li></ul>
<b>Type III</b> (immune complex)	Antibody-antigen complex deposition	<ul style="list-style-type: none"><li>• Serum sickness</li><li>• Poststreptococcal glomerulonephritis</li><li>• Lupus nephritis</li></ul>
<b>Type IV</b> (delayed type)	T cell- & macrophage-mediated	<ul style="list-style-type: none"><li>• Contact dermatitis</li><li>• Tuberculin skin test</li></ul>



New | Existing







defense against cutaneous infections (eg, cellulitis, which is painful rather than pruritic), this patient's rash is more consistent with contact dermatitis.

**(Choice D)** Immunoglobulins produced by plasma cells are responsible for **type II and III** hypersensitivity reactions. ACD does not involve plasma cells or antibodies.

**(Choice E)** Regulatory T cells are CD4<sup>+</sup> lymphocytes that play an inhibitory role in the immune response. They secrete cytokines (eg, interleukin-10) that inhibit macrophage function and antagonize proinflammatory cytokines (eg, interferon gamma). This anti-inflammatory effect is important in suppressing autoimmune diseases.

### Educational objective:

Allergic contact dermatitis is a type IV (delayed-type) hypersensitivity reaction. Initially, Langerhans cells present haptens to naive T cells, leading to clonal expansion. On reexposure, sensitized CD8<sup>+</sup> T cells are recruited to skin and destroy tissue. Release of interferon gamma by T cells further amplifies the immune response.

### References

- **Type IV hypersensitivity reaction.**





A 36-year-old man comes to the office to discuss a skin rash on his shoulders and upper chest. The patient first noticed the rash 2 months ago while vacationing at a beach resort. The rash has worsened progressively and is associated with mild pruritus, but he has no other associated symptoms. The patient is a road construction worker, and often works in hot, humid areas. Past medical history is notable for seasonal allergies and childhood asthma. He does not use tobacco or alcohol. Skin examination findings are shown in the image below.





Item 14 of 40

Question Id: 104



Mark



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Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



Which of the following is the most likely cause of this patient's condition?

Block Time Remaining: 00:48:01

TUTOR

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Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings



Which of the following is the most likely cause of this patient's condition?

- ☐ A. *Blastomyces dermatitidis*
- ☐ B. *Candida albicans*
- ☐ C. *Histoplasma capsulatum*
- ☐ D. *Malassezia globosa*
- ☐ E. *Microsporum canis*
- ☐ F. *Rhizopus species*
- ☐ G. *Sporothrix schenckii*



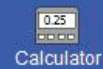
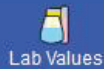
Feedback



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Which of the following is the most likely cause of this patient's condition?

- ☐ A. *Blastomyces dermatitidis* (8%)
- ☐ B. *Candida albicans* (3%)
- ☐ C. *Histoplasma capsulatum* (1%)
- ☒ D. *Malassezia globosa* (75%)
- ☐ E. *Microsporum canis* (6%)
- ☐ F. *Rhizopus species* (2%)
- ☐ G. *Sporothrix schenckii* (2%)

Correct



75%



51 secs



12/18/2020

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Mark



Previous



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Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Medically important fungi	
Cutaneous	<ul style="list-style-type: none"><li>• Dermatophytosis (eg, tinea, onychomycosis)</li><li>• Pityriasis versicolor</li></ul>
Subcutaneous	<ul style="list-style-type: none"><li>• Sporotrichosis</li></ul>
Systemic	<ul style="list-style-type: none"><li>• Histoplasmosis</li><li>• Coccidioidomycosis</li><li>• Blastomycosis</li></ul>
Opportunistic	<ul style="list-style-type: none"><li>• <i>Candida</i></li><li>• <i>Aspergillus</i></li><li>• <i>Mucor</i></li><li>• <i>Rhizopus</i></li></ul>

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**Pityriasis versicolor** (also called tinea versicolor) is characterized by hypopigmented, hyperpigmented, or erythematous macules or patches on the upper body. It is caused by *Malassezia* species yeasts, and the infection is confined to the **stratum corneum** of the skin. It is common in areas with hot and humid climates and is often most **visible after** extensive sun exposure due to **tanning of the adjacent skin**.



1



Feedback



Suspend



End Block



climates and is often most **visible after** extensive sun exposure due to **tanning of the adjacent skin**.

Most cases of pityriasis versicolor occur in healthy individuals with no underlying immunologic deficiencies.

The diagnosis of pityriasis versicolor is made by potassium hydroxide (**KOH**) **preparation** of skin scrapings. *Malassezia* forms spores and hyphae, producing the characteristic "**spaghetti and meatballs**" appearance on light microscopy. The hyphae have a short, "cigar-butt" appearance. This condition is treated with topical antifungal agents or selenium-containing shampoo.

**(Choices A and C)** Blastomycosis is characterized by progressive pulmonary infection. Skin involvement is uncommon but can manifest as papular or pustular lesions in exposed areas. Histoplasmosis also most commonly causes pulmonary disease, though it may become disseminated in immunodeficient patients.

**(Choice B)** *Intertrigo* is characterized by well-defined erythematous plaques with satellite vesicles or pustules in warm, moist skin areas (eg, axillae, groin, skin folds). The infection is usually due to *Candida* species, and it is most common following antibiotic use or in immunocompromised states (eg, uncontrolled diabetes).

**(Choice E)** *Microsporum* species are a frequent cause of *tinea capitis* and *tinea corporis*.

**(Choice F)** *Rhizopus* is a major cause of *mucormycosis*, which is characterized by invasive, necrotic upper and lower respiratory infections in immunocompromised patients.

climates and is often most visible after extensive sun exposure due to tanning of the adjacent skin

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

and lower respiratory infections in immunocompromised patients.

climates and is often most visible after extensive sun exposure due to tanning of the adjacent skin

Exhibit Display



Zoom In Zoom Out Reset New Existing My Notebook

and lower respiratory infections in immunocompromised patients.



climates and is often most visible after extensive sun exposure due to tanning of the adjacent skin

Exhibit Display



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and lower respiratory infections in immunocompromised patients.

climates and is often most visible after extensive sun exposure due to tanning of the adjacent skin

Exhibit Display



Zoom In Zoom Out Reset New | Existing My Notebook

and lower respiratory infections in immunocompromised patients.

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Feedback

Suspend

End Block

(Choice B) *Intertrigo* is characterized by well-defined erythematous plaques with satellite vesicles or pustules in warm, moist skin areas (eg, axillae, groin, skin folds). The infection is usually due to *Candida* species, and it is most common following antibiotic use or in immunocompromised states (eg, uncontrolled diabetes).

(Choice E) *Microsporum* species are a frequent cause of *tinea capitis* and *tinea corporis*.

(Choice F) *Rhizopus* is a major cause of *mucormycosis*, which is characterized by invasive, necrotic upper and lower respiratory infections in immunocompromised patients.

(Choice G) *Sporothrix* molds are found in decaying horticultural matter and are acquired through breaks in the skin. They cause nodular and ulcerating subcutaneous lesions.

### Educational objective:

Pityriasis versicolor (tinea versicolor) is a superficial skin infection caused by *Malassezia* species. It causes erythematous, hyper- or hypopigmented macules and patches. *Malassezia* forms spores and hyphae, producing the characteristic "spaghetti and meatballs" appearance on KOH preparation light microscopy.

### References

- [Microreview of pityriasis versicolor and Malassezia species.](#)



(Choice B) Intertrigo is characterized by well-defined erythematous plaques with satellite vesicles or

Exhibit Display



A 35-year-old man comes to the physician with a skin rash. He was treated in the hospital for pneumocystic pneumonia and painful oral ulcers 6 months ago. He currently takes no medications but drinks alcohol frequently and uses illicit drugs. Physical examination shows a widespread rash consisting of lesions similar to that shown in the image below.





Which of the following is the most likely cause of this patient's current condition?

- ☐ A. Arsenic exposure
- ☐ B. Cytomegalovirus
- ☐ C. Epstein-Barr virus
- ☐ D. Hepatitis C virus
- ☐ E. Herpes simplex virus type 1
- ☐ F. Human herpes virus type 8
- ☐ G. Human papilloma virus
- ☐ H. Human T-cell leukemia virus type 1
- ☐ I. Ultraviolet radiation
- ☐ J. Vinyl chloride exposure







Mark

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Which of the following is the most likely cause of this patient's current condition?

- ☐ A. Arsenic exposure (0%)
- ☐ B. Cytomegalovirus (2%)
- ☐ C. Epstein-Barr virus (3%)
- ☐ D. Hepatitis C virus (2%)
- ☐ E. Herpes simplex virus type 1 (2%)
- ☒ F. Human herpes virus type 8 (77%)
- ☐ G. Human papilloma virus (1%)
- ☐ H. Human T-cell leukemia virus type 1 (7%)
- ☐ I. Ultraviolet radiation (1%)
- ☐ J. Vinyl chloride exposure (0%)

Correct

77%

48 secs

11/18/2020

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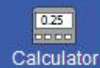
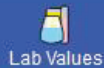
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Feedback

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The clinical history of pneumocystic pneumonia and painful oral ulcers in an illicit drug user is highly suggestive of HIV infection, a diagnosis further supported by the presence of Kaposi's sarcoma (KS).

The most common tumor in HIV-positive individuals, KS presents as multiple blue-violet or brownish dermal plaques that first appear on the feet and legs before spreading proximally. KS lesions can also develop on the mucosal membranes of the face and genitals. In patients with late-stage disease, the lesions spread to the lungs and gastrointestinal tract. Histologic examination of skin afflicted with **Kaposi's sarcoma** shows spindle and endothelial cell proliferation, red blood cell extravasation, and inflammation.

KS is strongly associated with both HIV and the human herpes virus type 8 (HHV-8); HHV-8 DNA has been isolated in the neoplastic cells of KS. HHV-8 infects vascular and lymphatic endothelial cells, causing their differentiation into a mixed phenotype that is thought to increase oncogenic potential. The HHV-8 genome also contains several viral oncogenes that inhibit both cell cycle regulation and apoptosis, thus promoting tumorigenesis.

**(Choice B)** Cytomegalovirus (CMV) infection in HIV patients typically cause esophagitis, colitis, and retinitis. CMV can also cause a mononucleosis like illness with rash; but the rash usually has a maculopapular/morbilliform appearance.

**(Choice C)** Like HHV-8, Epstein Barr virus also belongs to *Herpesviridae*. Epstein Barr virus causes





Mark



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Lab Values



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Reverse Color

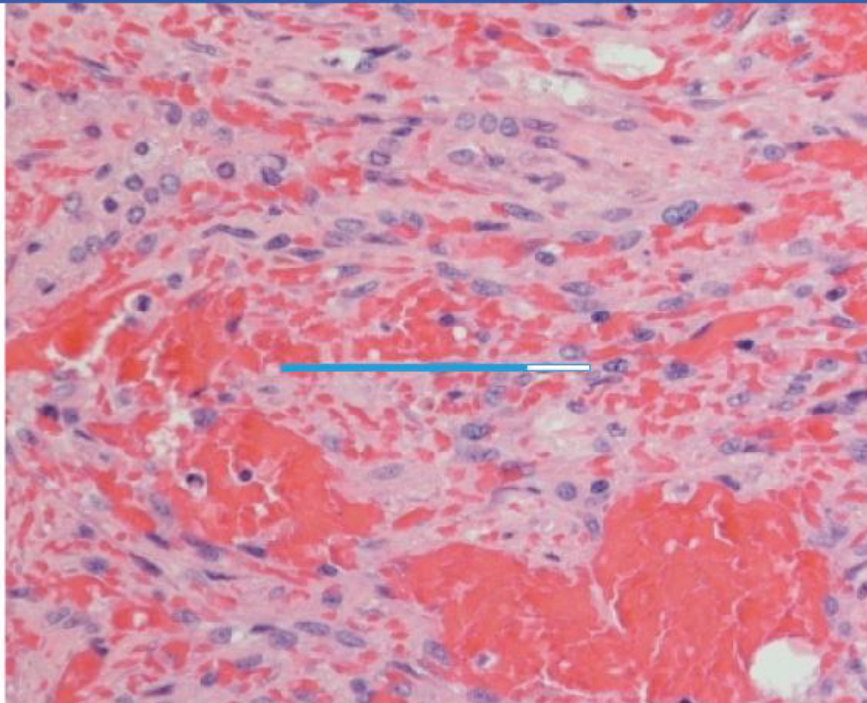


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(Choice C) Like HHV-8, Epstein-Barr virus also belongs to *Hermesviridae*. Epstein-Barr virus causes

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**(Choice C)** Like HHV-8, Epstein-Barr virus also belongs to *Herpesviridae*. Epstein-Barr virus causes infectious mononucleosis and is associated with Burkitt lymphoma, nasopharyngeal carcinoma, and central nervous system lymphoma in HIV-positive patients.

**(Choice D)** Chronic infection with hepatitis C virus increases the risk of developing hepatocellular carcinoma.

**(Choice G)** Human papilloma virus strains 16, 18, 31, and 33 are associated with squamous cell carcinoma of the cervix and vulva.

**(Choice H)** Human T-cell leukemia virus type 1 (HTLV-1) belongs to *Retroviridae*. It causes T-cell leukemia, especially in patients originating from southern Japan.

### Educational objective:

Kaposi's sarcoma typically presents as blue-violet or brownish skin plaques on the extremities and mucous membranes of HIV-positive patients. This tumor arises from primitive mesenchymal cells and is strongly associated with human herpes virus type 8.

### References

- Lymphatic reprogramming by Kaposi sarcoma herpes virus promotes the oncogenic activity of the virus-encoded G protein-coupled receptor





A 62-year-old man is brought to the emergency department from a homeless shelter due to alcohol intoxication. The patient has no other symptoms or history of significant medical conditions. Examination of the scalp reveals the findings shown in the [exhibit](#). Which of the following organisms is most likely responsible for this patient's condition?

- ☐ A. *Cimex lectularius*
- ☐ B. *Malassezia* species
- ☐ C. *Pediculus humanus capitis*
- ☐ D. *Phthirus pubis*
- ☐ E. *Sarcoptes scabiei*
- ☐ F. *Trichophyton tonsurans*

Submit





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Question Id: 17230



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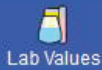
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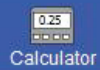
Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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### Exhibit Display



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A 62-year-old man is brought to the emergency department from a homeless shelter due to alcohol intoxication. The patient has no other symptoms or history of significant medical conditions. Examination of the scalp reveals the findings shown in the [exhibit](#). Which of the following organisms is most likely responsible for this patient's condition?

- ☐ A. *Cimex lectularius* (2%)
- ☐ B. *Malassezia* species (8%)
- ✓ ☐ C. *Pediculus humanus capitis* (70%)
- ☐ D. *Phthirus pubis* (4%)
- ✗ ☒ E. *Sarcoptes scabiei* (9%)
- ☐ F. *Trichophyton tonsurans* (5%)

**Incorrect**

Correct answer

C



70%

Answered correctly



23 secs

Time Spent



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This patient has numerous **nits**, which are egg casings of the **head louse** *Pediculus humanus capitis*.

**Pediculosis capitis** (ie, head lice infestation) is common in school children and adults who come into close contact with infested individuals (eg, sports teams, homeless shelters). Transmission is usually by **direct contact**, although transmission by fomites (eg, hats, hairbrushes) can also occur. Head lice require multiple blood meals a day and die within 2 days if separated from a host. They do not carry arthropod-borne infection, but the bite can induce a pruritic allergic reaction.

Female lice attach their nits to the hair shaft about 0.5 cm from the skin surface; nits further from the surface often represent old egg casings that have hatched and generally do not require treatment. First-line treatment includes **topical pediculicides** (eg, permethrin, ivermectin). Manual lice removal via **wet combing** is an alternate treatment for patients for whom standard pediculicides are not feasible (eg, children age <2 years, resource-poor populations).

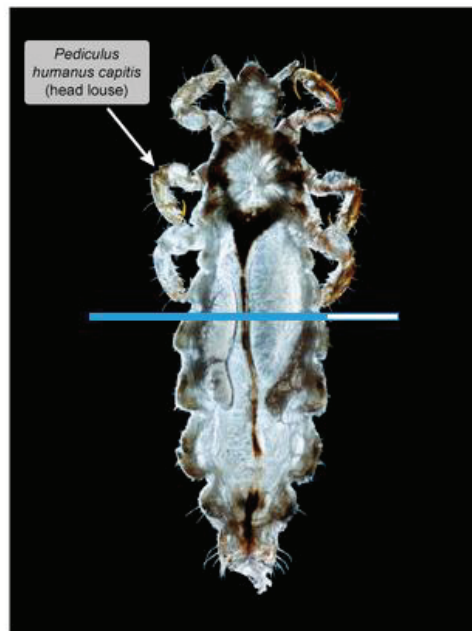
**(Choice A)** *Cimex lectularius* (ie, bedbugs) bites present as pruritic, red papules in clusters. The females lay eggs away from the host and do not produce nits.

**(Choice B)** Colonization with *Malassezia* yeasts is associated with seborrheic dermatitis. On the scalp, this condition can produce white skin flakes in the hair (ie, dandruff). The flakes are not adherent to the



### Exhibit Display

#### Pediculosis capitis



*Pediculus  
humanus capitis*  
(head louse)

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this condition can produce white skin flakes in the hair (ie, dandruff). The flakes are not adherent to the hair shaft and are typically found loosely throughout the hair and on the clothing.

**(Choice D)** *Pthirus pubis* (ie, crab louse, pubic louse) is usually transmitted by sexual contact. The louse is adapted for attaching to thick hair shafts, and the nits are usually found on pubic and other thick hair (eg, eyelashes); however, scalp hair is not typically affected.

**(Choice E)** *Sarcoptes scabiei* causes scabies, which presents with pruritic papules and burrows on the interdigital and flexural skin of the extremities. The female mite lays eggs in burrows and does not form nits.

**(Choice F)** *Trichophyton tonsurans* is a dermatophyte that causes tinea capitis, which presents as a scaly, erythematous patch of hair loss. There are often small, black dots that represent broken hair shafts.

### Educational objective:

*Pediculus humanus capitis* (ie, head lice) infestation is common in school children and adults who come into close contact with infested individuals. Transmission is usually by direct contact. The eggs (nits) are attached to the hair shaft and can be identified on inspection. First-line treatment includes topical pediculicides (eg, permethrin, ivermectin).





A 35-year-old man comes to the office for evaluation of red skin lesions under his nipple that were first noticed by his wife. The lesions are not itchy or painful, and no other family members have skin lesions. He has not used any new soaps, lotions, or detergents. The patient has no known medical problems and takes no medications. He drinks 4-6 beers every night. He does not use tobacco or illicit drugs. Body mass index is 32kg/m<sup>2</sup>, and vital signs are normal. The skin findings are shown below.





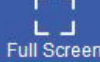
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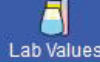
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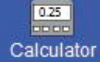
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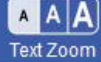
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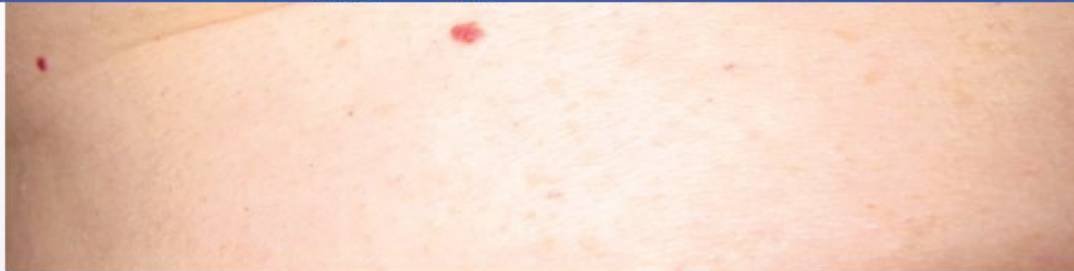
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Which of the following is the most likely diagnosis in this patient?

- ☐ A. Acrochordon
- ☐ B. Cavernous hemangioma
- ☐ C. Cherry hemangioma
- ☐ D. Cystic hygroma
- ☐ E. Spider angioma
- ☐ F. Strawberry hemangioma

**Submit**

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Which of the following is the most likely diagnosis in this patient?

- ☐ A. Acrochordon (2%)
- ☐ B. Cavernous hemangioma (4%)
- ☒ C. Cherry hemangioma (77%)
- ☐ D. Cystic hygroma (0%)
- ☐ E. Spider angioma (2%)
- ☐ F. Strawberry hemangioma (11%)





This patient's **small, bright-red**, papular lesions are **cherry hemangiomas**, also known as cherry angiomas or senile hemangiomas. They are the most common **benign vascular tumors in adults** and typically appear during the third or fourth decade of life. The lesions do not regress spontaneously and often **multiply** with age. Cherry hemangiomas are always superficial on the skin and are not found on the mucosa or deep tissues. Histologically, they appear as sharply circumscribed areas of congested capillaries and post-capillary venules in the papillary dermis.

**(Choice A)** Acrochordons (skin tags) are pedunculated outgrowths of normal skin. They are typically seen in areas of friction (eg, neck, axilla, inframammary, groin) of patients with obesity and diabetes mellitus.

**(Choice B)** Cavernous hemangiomas consist of dilated vascular spaces with thin-walled endothelial cells. They present as soft blue, compressible masses up to a few centimeters in size. They may appear on the skin, mucosa, deep tissues, and viscera. When cavernous hemangiomas appear on the skin, they are most frequently based in the dermis.

**(Choice D)** Cystic hygromas are comprised of lymphatic cysts lined by a thin endothelium. These benign tumors are often present at birth and are most commonly located on the posterior neck and lateral chest wall. Cystic hygromas are frequently found in neonates with Turner syndrome and Down syndrome.



Exhibit Display



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**(Choice D)** Cystic hygromas are comprised of lymphatic cysts lined by a thin endothelium. These benign tumors are often present at birth and are most commonly located on the posterior neck and lateral chest wall. Cystic hygromas are frequently found in neonates with Turner syndrome and Down syndrome.

**(Choice E)** Spider angiomas consist of a bright red central papule surrounded by several outwardly radiating vessels that blanch with pressure and refill centrifugally upon release. They are associated with increased estrogen states (eg, pregnancy, cirrhosis, oral contraceptive use, estrogen supplement use).

**(Choice F)** Strawberry (also known as infantile or capillary) hemangiomas appear during the first weeks of life. They initially grow rapidly and then frequently regress spontaneously by late childhood. They are bright red when near the epidermis and more violaceous when deeper.

### Educational objective:

Cherry hemangiomas are small, red, cutaneous papules common in aging adults. They do not regress spontaneously and typically increase in number with age. Light microscopy of these lesions shows proliferation of capillaries and post-capillary venules in the papillary dermis.

### References

- [Diagnosis and management of infantile hemangiomas.](#)





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(Choice D) Cystic hygromas are comprised of lymphatic cysts lined by a thin endothelium. These benign

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A 26-year-old male with a history of childhood dermatitis, asthma, and hay fever has routinely been applying a corticosteroid cream to the flexor areas of his skin for many years. The treated areas have remained free of erythema, papules, vesicles, crusts, or scales. A punch biopsy from one of the areas subjected to this topical therapy would most likely show which of the following?

- ☐ A. Intraepidermal vesicles
- ☐ B. Epidermal hyperkeratosis
- ☐ C. Epidermal hyperplasia
- ☐ D. Dermal atrophy
- ☐ E. Dermal perivascular lymphocytosis
- ☐ F. Adipose tissue hyperplasia

Submit







A 26-year-old male with a history of childhood dermatitis, asthma, and hay fever has routinely been applying a corticosteroid cream to the flexor areas of his skin for many years. The treated areas have remained free of erythema, papules, vesicles, crusts, or scales. A punch biopsy from one of the areas subjected to this topical therapy would most likely show which of the following?

- ☐ A. Intraepidermal vesicles (3%)
- ☐ B. Epidermal hyperkeratosis (16%)
- ☐ C. Epidermal hyperplasia (7%)
- ☒ D. Dermal atrophy (58%)
- ☐ E. Dermal perivascular lymphocytosis (6%)
- ☐ F. Adipose tissue hyperplasia (7%)

Correct



58%  
Answered correctly



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This patient has been successfully treated for atopic eczematous dermatitis. Hence, marked histological manifestations of active eczema such as intraepidermal vesicles, superficial epidermal hyperkeratosis producing scales, epidermal hyperplasia (acanthosis), and/or a chronic inflammatory infiltrate within the dermis would not be expected. This dermatitis cure comes with a price, however; along with anti-inflammatory actions, corticosteroids decrease the production of extracellular matrix collagen and glycosaminoglycans. Consequences include atrophy of the dermis with loss of dermal collagen, drying, cracking, and/or tightening of the skin. Telangiectasias, ecchymoses from mild trauma, and atrophic striae may also be found.

**(Choice F)** Via an uncertain mechanism, chronic application of topical corticosteroids may also cause atrophy, not hyperplasia, of subcutaneous tissues, including adipocytes.

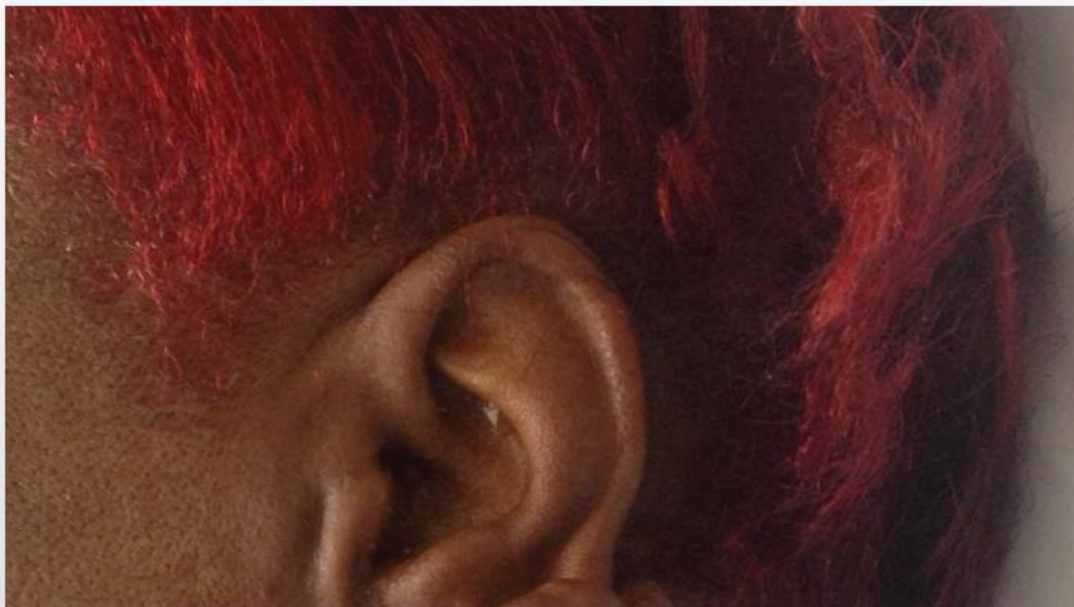
### **Educational Objective:**

Local cutaneous adverse effects of chronic topical corticosteroid administration include atrophy/thinning of the dermis that is associated with loss of dermal collagen, drying, cracking, and/or tightening of the skin, telangiectasias, and ecchymoses.





An 18-year-old woman comes to the office due to a slowly enlarging, irregularly shaped mass on her left ear. The mass is often itchy and painful. She had an ear piercing at this site 6 months ago, but there were no immediate complications such as bleeding. The patient has smaller, similar lesions on her right knee and elbow that have been present for several years. Her ear is shown in the image below.







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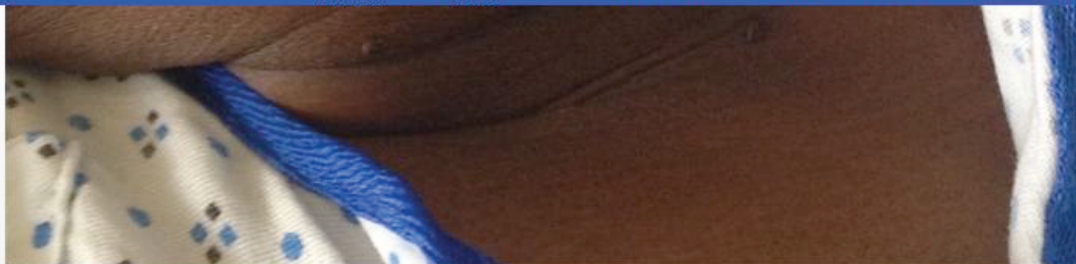


Which of the following is most likely responsible for this patient's lesion?

- ☐ A. Chronic venous insufficiency
- ☐ B. Defective type V collagen
- ☐ C. Excess collagen formation
- ☐ D. Healing by primary intention
- ☐ E. Retained foreign body
- ☐ F. Wound contraction

Submit





Which of the following is most likely responsible for this patient's lesion?

- ☐ A. Chronic venous insufficiency (0%)
- ☐ B. Defective type V collagen (1%)
- ☒ C. Excess collagen formation (94%)
- ☐ D. Healing by primary intention (1%)
- ☐ E. Retained foreign body (0%)
- ☐ F. Wound contraction (1%)







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## Normal wound healing

Phase	Timeline (after injury)	Characteristics
Hemostasis	0-1 day	<ul style="list-style-type: none"><li>• Vasoconstriction, platelet aggregation, fibrin deposition</li></ul>
Inflammatory	1-3 days	<ul style="list-style-type: none"><li>• Neutrophil migration &amp; macrophage phagocytosis of necrotic debris &amp; bacterial contaminants</li></ul>
Proliferative	3 days - 3 weeks	<ul style="list-style-type: none"><li>• Formation of granulation tissue:<ul style="list-style-type: none"><li>○ Fibroblasts begin to form connective tissue</li><li>○ Endothelial cells begin to form blood vessels (neovascularization)</li></ul></li><li>• Wound contraction</li></ul>
Maturation (remodeling)	3 weeks - several months	<ul style="list-style-type: none"><li>• Fibroblasts continue to synthesize connective tissue matrix (eg, collagen, elastin)</li><li>• Slow, progressive increase in tensile strength of new tissue</li></ul>

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**Excessive collagen formation** during the remodeling phase of wound healing can result in a **keloid** or hypertrophic scar. Keloids and hypertrophic scars consist of connective tissue rich in fibroblasts, myofibroblasts, and bundles of collagen fibers that are arranged in a **disorganized fashion** (black arrow) in keloids and in parallel in hypertrophic scars.

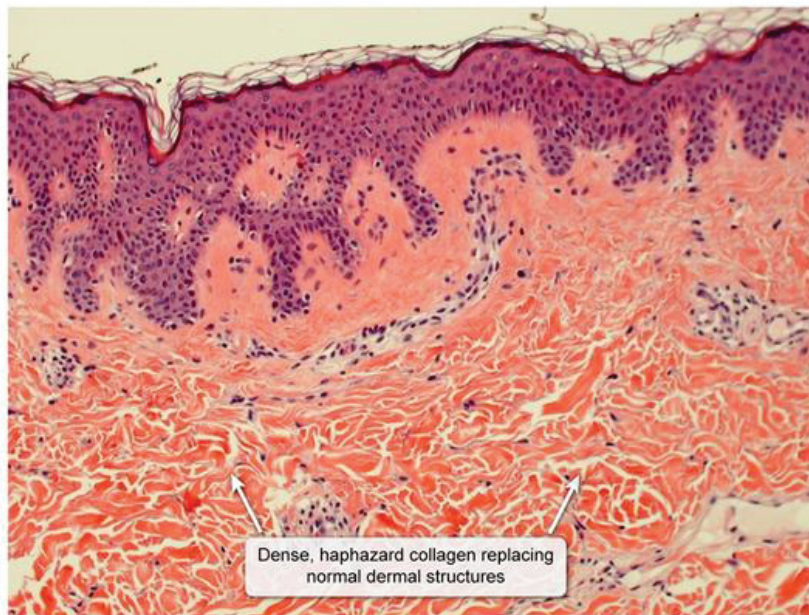
Normally, wound contraction (**Choice F**), a normal part of the proliferative phase of wound healing, involves contraction of actin in myofibroblasts to approximate wound edges. Transformation growth factor-beta (TGF- $\beta$ ) promotes differentiation of fibroblasts into myofibroblasts and should diminish on completion of wound repair. In keloids, TGF- $\beta$  is produced excessively without regulation. As a result, keloids **extend beyond the borders** of the original wound, do not regress, and often recur after resection. They arise following minor (eg, ear piercing) or major (eg, full-thickness burn) trauma and can be **raised, painful**, and **pruritic**. Keloids can have a familial tendency, particularly in persons of Asian or African ethnicity. Unlike keloids, hypertrophic scars are limited to the wound area and may regress spontaneously.

**(Choice A)** Chronic venous insufficiency is characterized by valvular incompetency and venous hypertension which lead to an overactive inflammatory response. The chronic release of inflammatory markers increases vascular permeability, resulting in edema, and proteolytic enzymes cause chronic ulceration.



## Exhibit Display

## Keloid



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ulceration.

**(Choice B)** Ehlers-Danlos is a connective tissue disorder that classically involves a genetic mutation of type V collagen. This leads to joint hypermobility and skin hyperelasticity and fragility. Due to defective collagen production, wound healing is impaired (eg, frequent dehiscence, longer remodeling phase).

**(Choice D)** Healing by [primary intention](#) describes surgical closure of well-approximated wound edges, which decreases the likelihood of significant scarring. In contrast, wound healing by secondary intention (spontaneous healing) is more likely to lead to scarring and prolonged remodeling as the wound edges are not well approximated.

**(Choice E)** The presence of a foreign body in a wound can delay wound healing and increase the risk of infection. It does not increase the likelihood of keloid development.

### Educational objective:

Keloids result from excessive collagen formation during the remodeling phase of wound healing. They present as raised, painful, and pruritic nodules that grow beyond the wound borders.

### References

- [Functional histopathology of keloid disease.](#)
- [Nine-month-old patient with bilateral earlobe keloids](#)





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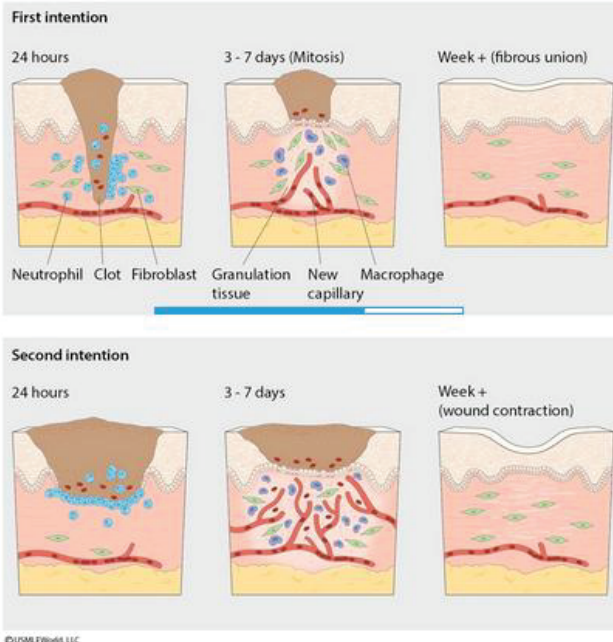


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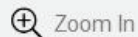
ulceration

## Exhibit Display

## Wound healing by first &amp; second intention



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• Nine-month-old patient with bilateral earlobe keloids

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A 38-year-old woman comes to the urgent care clinic with a 2-day history of sore throat. It is associated with fever and cervical lymphadenopathy, but not rhinorrhea, sneezing, or coughing. On examination, erythema and edema involving the posterior pharynx and a purulent tonsillar exudate are present. Rapid bedside streptococcal antigen testing is positive, and the patient is started on oral penicillin V. She returns the following day with a pruritic skin rash that came on suddenly after starting the antibiotic. The skin lesions observed on physical examination are shown in the image below.





lesions observed on physical examination are shown in the image below.



What is the most likely finding on biopsy of these lesions?



What is the most likely finding on biopsy of these lesions?

- ☐ A. Acantholysis
- ☐ B. Acanthosis
- ☐ C. Dermal edema
- ☐ D. Dyskeratosis
- ☐ E. Epidermal spongiosis

Submit





What is the most likely finding on biopsy of these lesions?

- ☐ A. Acantholysis (7%)
- ☐ B. Acanthosis (4%)
- ☒ C. Dermal edema (60%)
- ☐ D. Dyskeratosis (1%)
- ☐ E. Epidermal spongiosis (25%)

Correct

60%



19 secs



01/18/2021

Block Time Remaining: 00:51:21

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**Urticaria** ("hives") is a common, transient **hypersensitivity** disorder characterized by intensely pruritic, raised, erythematous plaques (**wheals**) that arise suddenly and resolve over several hours. They are most often caused by **IgE-mediated degranulation** of mast cells. They can also be due to non-IgE-mediated degranulation (eg, opiates, radiocontrast agents, physical urticaria) or mast cell-independent mechanisms (eg, aspirin, hereditary angioneurotic edema).

Urticaria is due to increased permeability of the microvasculature, leading to **edema** of the **superficial dermis**. Involvement of the deep dermis and subcutaneous tissue is termed angioedema. Biopsy is rarely required for diagnosis. Findings on histopathology would typically include a mixed inflammatory infiltrate (mononuclear cells, neutrophils, and eosinophils) surrounding superficial dermal venules. Lymphatic channels may be engorged with transudative fluid. The overlying epidermis typically appears normal.

**(Choice A)** Acantholysis is the loss of cohesion between keratinocytes in the epidermis. It is a characteristic finding in the pemphigus family of disorders.

**(Choice B)** Acanthosis is a diffuse increase in thickness of the stratum spinosum (prickle cell layer) between the granular cell layer and the basal layer of the epidermis. Common conditions displaying acanthosis include psoriasis, seborrheic dermatitis, and acanthosis nigricans.

**(Choice D)** Dyskeratosis describes the abnormal, premature keratinization of individual keratinocytes.





between the granular cell layer and the basal layer of the epidermis. Common conditions displaying acanthosis include psoriasis, seborrheic dermatitis, and acanthosis nigricans.

**(Choice D)** Dyskeratosis describes the abnormal, premature keratinization of individual keratinocytes.

Dyskeratotic cells are strongly eosinophilic and may have a small, basophilic nuclear remnant.

Dyskeratosis can be found in diseases such as squamous cell carcinoma.

**(Choice E)** Spongiosis is intercellular epidermal edema that histologically appears as an increase in the width of spaces between cells. Spongiosis is often associated with spongiotic dermatitis, which encompasses a number of conditions (eg, eczematous dermatitis).

### Educational objective:

Urticaria is a transient hypersensitivity disorder characterized by pruritic erythematous plaques that arise suddenly and resolve over hours. They are most often caused by IgE-mediated degranulation of mast cells, leading to increased permeability of the microvasculature with edema of the superficial dermis.

### References

- [Pathogenic intracellular and autoimmune mechanisms in urticaria and angioedema.](#)

Pathology

Dermatology

Urticaria





A 67-year-old man comes to the office after he noticed several nodules in his left axilla. He has a history of malignant melanoma on his upper back, which was treated with wide surgical excision 4 years ago. The patient undergoes biopsy of an axillary lesion, and histopathology reveals melanoma recurrence. Subsequent whole-body positron emission scan shows diffuse metastatic disease involving the lungs, liver, and left axillary nodes. Checkpoint inhibitor therapy with pembrolizumab is initiated, which leads to significant reduction in the size of the axillary nodules and metastatic lesions. Which of the following best correlates with the treatment response in this patient?

- ☐ A. Increased intratumor macrophages
- ☐ B. Intense desmoplastic reaction
- ☐ C. Ischemic tumor necrosis
- ☐ D. CD8+ lymphocyte infiltration
- ☐ E. Peritumoral neutrophilic reaction

**Submit**





A 67-year-old man comes to the office after he noticed several **nodules** in his **left axilla**. He has a history of **malignant melanoma** on his upper back, which was treated with wide surgical excision 4 years ago. The patient undergoes biopsy of an axillary lesion, and histopathology reveals melanoma recurrence. Subsequent whole-body positron emission scan shows **diffuse metastatic disease** involving the lungs, liver, and left axillary nodes. **Checkpoint inhibitor** therapy with **pembrolizumab** is initiated, which leads to significant reduction in the size of the axillary nodules and metastatic lesions. Which of the following best correlates with the treatment response in this patient?

- ☐ A. Increased intratumor macrophages (12%)
- ☐ B. Intense desmoplastic reaction (8%)
- ☐ C. Ischemic tumor necrosis (16%)
- ☒ D. CD8+ lymphocyte infiltration (57%)
- ☐ E. Peritumoral neutrophilic reaction (5%)

Correct

57%



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02/20/2021

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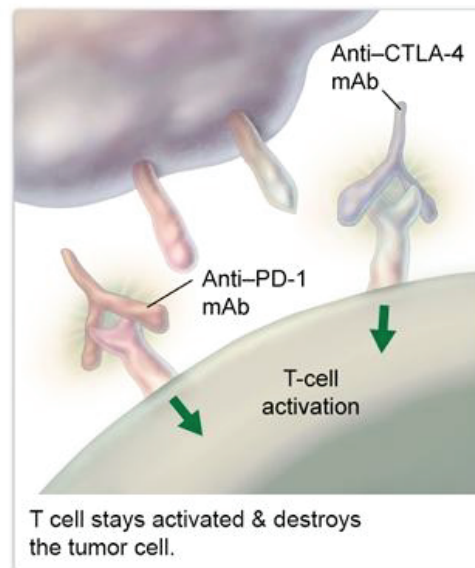
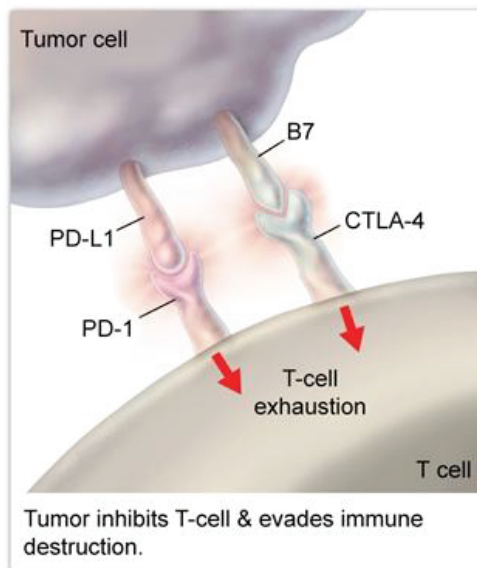


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End Block

### Cancer immunotherapy: anti-PD-1 & anti-CTLA-4 antibodies



CTLA-4 = cytotoxic T-lymphocyte-associated protein 4; mAb = monoclonal antibody;  
PD-1 = programmed death receptor-1; PD-L1 = programmed death ligand-1.

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Neoplastic cells produce proteins not found in healthy cells. Pieces of these proteins (**neoantigens**) are



Neoplastic cells produce proteins not found in healthy cells. Pieces of these proteins (**neoantigens**) are displayed on MHC class I molecules on the cell surface and are subsequently recognized by **cytotoxic T cells** as "nonself" (leading to cellular apoptosis). However, neoplastic cells generally accumulate genetic mutations that allow them to thwart the cytotoxic T-cell response and evade detection/destruction. One common mechanism is the overexpression of **programmed death-ligand 1** (PD-L1) on the cancer cell surface; this ligand binds to the PD-1 receptor on cytotoxic T cells and suppresses their ability to induce apoptosis (**T-cell exhaustion**).

Treatment with monoclonal antibodies that block PD-1 such as **pembrolizumab** have shown promise in cancers that overexpress PD-L1 (eg, **melanoma**, renal cell carcinoma). **Blockade of PD-1** restores the cytotoxic T-cell response (disinhibition), which **promotes tumor cell apoptosis**. Patients with advanced melanoma and other susceptible malignancies often have a drastic clinical response (eg, tumor regression, long-term remission) to PD-1 antagonists.

**(Choices A and E)** Cancer-related inflammation also involves cells of the innate immune system such as macrophages and neutrophils. These cells can have either protumor (eg, release of matrix metalloproteases that facilitate invasion) and antitumor (eg, direct killing of cancer cells) activities depending on the local cytokine milieu. However, PD-1 inhibitors do not increase the antitumor activity of neutrophils or macrophages.







metalloproteases that facilitate invasion) and antitumor (eg, direct killing of cancer cells) activities depending on the local cytokine milieu. However, PD-1 inhibitors do not increase the antitumor activity of neutrophils or macrophages.

**(Choice B)** Tumor cells often induce desmoplasia, which refers to excessive connective tissue/stroma growth around the tumor. A strong desmoplastic response can reduce the ability of chemotherapeutic agents to penetrate into the tumor, leading to chemoresistance.

**(Choice C)** Angiogenesis inhibitors (eg, bevacizumab) are used to prevent neovascularization of growing tumors, leading to ischemia and tumor necrosis. PD-1 inhibitors cause cytotoxic T-cell activation, leading to increased apoptosis of tumor cells; they do not induce ischemic necrosis.

### Educational objective:

Programmed-death receptor 1 (PD-1) is a checkpoint inhibitor that downregulates the cytotoxic T-cell response. Neoplastic cells often exploit this receptor via the overexpression of PD-1 ligand. PD-1 receptor inhibitors (eg, Pembrolizumab) restore the T-cell response, allowing cytotoxic T cells to invade the tumor and induce apoptosis of neoplastic cells.

Immunology

Dermatology

Melanoma





End Block

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Following pathologic sampling, the lesions are determined to be fungal in etiology. Which of the following scenarios is most likely a component of this patient's history?

- ☐ A. Animal contact
- ☐ B. Bat guano exposure
- ☐ C. Exposure to seawater
- ☐ D. Immune system disease
- ☒ E. Recent antibiotic use
- ☐ F. Thorn prick

Submit



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Following pathologic sampling, the lesions are determined to be fungal in etiology. Which of the following scenarios is most likely a component of this patient's history?

- ☐ A. Animal contact (5%)
- ☐ B. Bat guano exposure (4%)
- ☐ C. Exposure to seawater (1%)
- ☐ D. Immune system disease (6%)
- ☐ E. Recent antibiotic use (1%)
- ☒ F. Thorn prick (80%)

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This patient has a fungal dermatologic infection. The subcutaneous nodules pictured are consistent with **sporotrichosis**, a subcutaneous mycosis caused by *Sporothrix schenckii*. *Sporothrix* is a dimorphic **fungus** found in the natural environment in the form of mold (hyphae). It resides on the bark of trees, shrubs, and garden plants and on plant debris in soil. It enters the body through breaks in the skin (often via **thorn prick**) and spreads along the **lymphatics**. Sporotrichosis is commonly seen in gardeners.

The initial lesion - a reddish nodule that later ulcerates - appears at the site of the thorn prick or other skin injury. Biopsy of the lesion typically reveals a **granuloma** consisting of histiocytes, multinucleated giant cells, and neutrophils, surrounded by plasma cells. From the site of inoculation, the fungus spreads along the lymphatics, forming subcutaneous nodules and ulcers.

The diagnosis of sporotrichosis is made by culturing the affected area and isolating *S schenckii*. Antifungal therapy (eg, itraconazole) is needed.

**(Choice A)** Animal contact is associated with dermatophytoses caused by *Microsporum* species. *Microsporum canis* causes tinea capitis. Cat scratch disease (manifesting as a vesicle turning into a papule and accompanied by lymphadenopathy) is due to *Bartonella*, which is a gram-negative bacterium, not a fungus.

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**(Choice B)** Exposure to bats (eg, during cave exploration) or to bird droppings in the Ohio and Mississippi River Valley areas is associated with *Histoplasma capsulatum* infection, which typically causes lung disease resembling tuberculosis.

**(Choice C)** The bacterial organisms *Aeromonas* and *Vibrio vulnificus* may cause cellulitis related to freshwater or seawater exposure.

**(Choice D)** Immune system disease predisposes to systemic mycoses (eg, candidiasis, aspergillosis, mucormycosis). Sporotrichosis, in contrast, commonly affects immunocompetent individuals. Disseminated sporotrichosis is very rare.

**(Choice E)** Recent antibiotic use is associated with superficial *Candida* disease, such as oral thrush or vulvovaginitis.

**Educational objective:**

*Sporothrix schenckii* is a dimorphic fungus that causes a subcutaneous mycosis. It is often transmitted by a thorn prick. The disease manifests with nodules that spread along lymphatics.

Microbiology

Dermatology

Sporotrichosis

Subject

System

Topic

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A 65-year-old man comes to the office due to skin lesions on his back. He first noted the spots 5 years ago and says they are becoming more numerous. The lesions are occasionally pruritic but are otherwise asymptomatic. The patient did not come for evaluation previously because he "did not care about them," but made an appointment now at his wife's insistence. Medical history is notable for hypertension, hyperlipidemia, and type 2 diabetes mellitus. On examination, there are numerous pigmented plaques, as shown in the image below.



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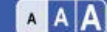
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Which of the following is the most likely diagnosis?

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Which of the following is the most likely diagnosis?

- ☐ A. Acanthosis nigricans
- ☐ B. Actinic keratosis
- ☐ C. Lichen planus
- ☐ D. Malignant melanoma
- ☐ E. Psoriasis
- ☐ F. Seborrheic keratosis

Submit

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Which of the following is the most likely diagnosis?

- ☐ A. Acanthosis nigricans (8%)
- ☐ B. Actinic keratosis (10%)
- ☐ C. Lichen planus (9%)
- ☐ D. Malignant melanoma (4%)
- ☐ E. Psoriasis (0%)
- ☒ F. Seborrheic keratosis (67%)

Correct

67%

18 secs

09/17/2020





**Seborrheic keratosis** (SK) (plural: keratoses) is a common, tan or brown, epidermal tumor occurring in middle-aged or elderly individuals. It has a variable appearance from nearly flat **macules** to raised, **wart-like** lesions, ranging in size from a few millimeters to centimeters. SK typically has a velvety or greasy surface and well-demarcated border, and is often described as having a "**stuck-on**" **appearance**. On **microscopic examination**, the lesions of SK are composed of small cells resembling basal cells, with variable pigmentation, hyperkeratosis (thickening of the stratum corneum), and keratin-containing cysts.

The etiology of SK is not fully understood; however, it is frequently associated with activating mutations of the **fibroblast growth factor receptor 3**. SK itself is benign, but **rapid onset of numerous SKs** (Leser-Trélat sign) is often associated with an **internal malignancy** (eg, gastric adenocarcinoma), possibly due to overproduction of insulin-like growth factor 1 and other cytokines.

**(Choice A)** Acanthosis nigricans is characterized by **hyperpigmented, velvety plaques** at flexural areas (eg, axilla, posterior neck). It is associated with diabetes mellitus, obesity, visceral malignancy, and various endocrinopathies.

**(Choice B)** Actinic keratosis presents with **hyperkeratotic lesions** in sun-exposed areas of the scalp, ears, face, and hands. These lesions are unpigmented and, despite the similar name, are unrelated to

seborrheic keratosis



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seborrheic keratosis

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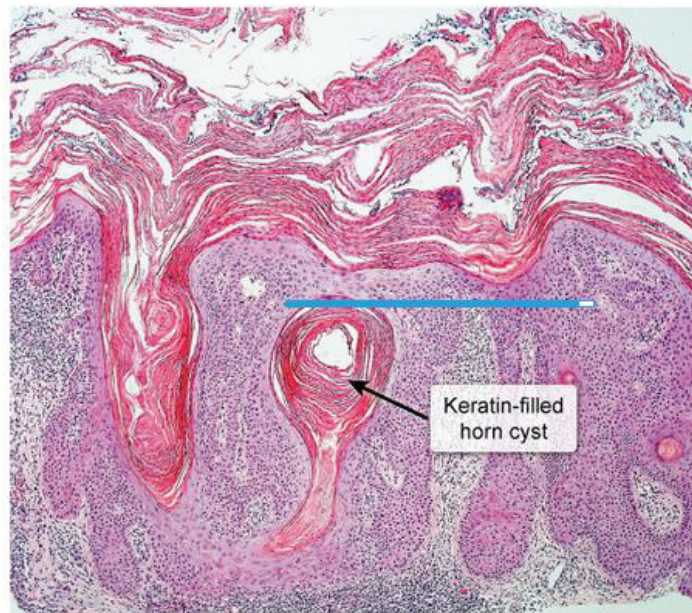
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## Exhibit Display

## Seborrheic keratosis



Hyperkeratosis

Thickened  
epidermis  
(acanthosis)Keratin-filled  
horn cyst

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**(Choice B)** Actinic keratosis presents with **hyperkeratotic lesions** in sun-exposed areas of the scalp, ears, face, and hands. These lesions are unpigmented and, despite the similar name, are unrelated to seborrheic keratosis.

**(Choice C)** Lichen planus is characterized by the "5 Ps": polygonal, planar, pruritic, **purplish plaques** on the wrists, hands, trunk, and legs. Fine white lines (Wickham striae) may be present on the plaque surface.

**(Choice D)** Melanoma characteristically presents as an **asymmetric, pigmented lesion** with an irregular border, variable coloration, and change in size and appearance over time. Multifocal development of monotonous, otherwise asymptomatic lesions is much more typical of SK.

**(Choice E)** Psoriasis presents with scaly, nonpigmented plaques. Although it may occur on the trunk, it is more common on the extensor surfaces of the extremities.

### Educational objective:

Seborrheic keratosis is a common epidermal tumor that presents as a tan or brown, round lesion with a well-demarcated border and "stuck-on" appearance. Microscopic examination shows small cells resembling basal cells, with pigmentation, hyperkeratosis, and keratin-containing cysts. Rapid onset of numerous lesions is often associated with internal malignancy (Leser-Trélat sign).



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A 23-year-old Caucasian male who notes recurrent severe nosebleeds is found to have pink spider-like lesions on his oral and nasal mucosa, face, and arms. The patient most likely suffers from:

- ☐ A. Von Recklinghausen's disease
- ☐ B. Neurofibromatosis type 2
- ☐ C. Sturge-Weber syndrome
- ☐ D. Von Hippel-Lindau disease
- ☐ E. Tuberous sclerosis
- ☐ F. Osler-Weber-Rendu syndrome

Submit





A 23-year-old Caucasian male who notes recurrent severe nosebleeds is found to have pink spider-like lesions on his oral and nasal mucosa, face, and arms. The patient most likely suffers from:

- ☐ A. Von Recklinghausen's disease (5%)
- ☐ B. Neurofibromatosis type 2 (2%)
- ☐ C. Sturge-Weber syndrome (15%)
- ☐ D. Von Hippel-Lindau disease (9%)
- ☐ E. Tuberous sclerosis (6%)
- ☒ F. Osler-Weber-Rendu syndrome (60%)

Correct



60%  
Answered correctly



55 secs  
Time Spent



01/30/2021  
Last Updated

Explanation





This patient presents with skin and mucosal telangiectasias as well as recurrent severe nosebleeds. The most likely diagnosis is Osler-Weber-Rendu syndrome (hereditary hemorrhagic telangiectasia), a condition characterized by the autosomal dominant inheritance of congenital telangiectasias to the skin and mucous membranes. The mucosal involvement may affect the lips, oronasopharynx, respiratory tract, gastrointestinal tract, or urinary tract. In rare instances, the telangiectasias of Osler-Weber-Rendu syndrome may occur in the brain, liver, and spleen as well. Rupture of these telangiectasias may cause epistaxis, gastrointestinal bleeding, and hematuria.

**(Choice A)** Von Recklinghausen's disease, or neurofibromatosis type 1 (NF1), is an inherited *peripheral nervous system* tumor syndrome. Patients develop neurofibromas, optic nerve gliomas, Lisch nodules (pigmented nodules of the iris), and café au lait spots (hyperpigmented cutaneous macules).

**(Choice B)** Neurofibromatosis type 2 is an autosomal dominant nervous system tumor syndrome, in which patients commonly develop bilateral cranial nerve VIII schwannomas and multiple meningiomas.

**(Choice C)** Sturge-Weber syndrome (encephalotrigeminal angiomas) is a rare congenital neurocutaneous disorder characterized by the presence of cutaneous facial angiomas as well as leptomeningeal angiomas. This condition is associated with mental retardation, seizures, hemiplegia, and



leptomeningeal angiomas. This condition is associated with mental retardation, seizures, hemiplegia, and skull radiopacities. Skull radiographs may show characteristic "tram-track" calcifications.

**(Choice D)** Von Hippel–Lindau disease is a rare, autosomal dominant condition characterized by the presence of capillary hemangioblastomas in the retina and/or cerebellum, as well as congenital cysts and/or neoplasms in the kidney, liver, and pancreas. Patients are also at increased risk for renal cell carcinoma, which can be bilateral.

**(Choice E)** Although tuberous sclerosis (TS) may cause kidney, liver, and pancreatic cysts, central nervous system (CNS) involvement manifests not as angiomatous lesions, but as cortical and subependymal *hamartomas*. This autosomal dominant syndrome is also characterized by cutaneous angiofibromas (adenoma sebaceum), visceral cysts, and a variety of other hamartomas, as well as renal angiomyolipomas and cardiac rhabdomyomas. Clinically, seizures are a major complication.

### Educational Objective:

Osler-Weber-Rendu syndrome (hereditary hemorrhagic telangiectasia) is an autosomal dominant condition marked by the presence of telangiectasias in the skin as well as the mucous membranes of the lips, oronasopharynx, respiratory tract, gastrointestinal tract, and urinary tract. Rupture of these telangiectasias may cause epistaxis, gastrointestinal bleeding, or hematuria.





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An 8-year-old boy is brought to the office due to a lower extremity skin rash for the past 3 days. The rash began as tender papules that quickly progressed to form vesicles and flaccid bullae that rupture easily. The patient has no mucosal lesions or other rashes and has never had similar symptoms before. He is up to date with recommended vaccinations and takes no medications. Skin examination findings are shown below.





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Which of the following is the most likely cause of this patient's skin findings?

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Which of the following is the most likely cause of this patient's skin findings?

- ☐ A. Autoantibodies targeted against hemidesmosomes
- ☐ B. Autoantibody-mediated epidermal cell separation
- ☐ C. Bacterial toxin-induced desmoglein 1 cleavage
- ☐ D. Defective epidermal barrier and T-cell dysregulation
- ☐ E. Inflammatory response to viral lytic infection

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Which of the following is the most likely cause of this patient's skin findings?

- ☐ A. Autoantibodies targeted against hemidesmosomes (13%)
- ☐ B. Autoantibody-mediated epidermal cell separation (20%)
- ☒ C. Bacterial toxin-induced desmoglein 1 cleavage (52%)
- ☐ D. Defective epidermal barrier and T-cell dysregulation (3%)
- ☐ E. Inflammatory response to viral lytic infection (10%)

Correct

52%  
Answered correctly

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Time Spent

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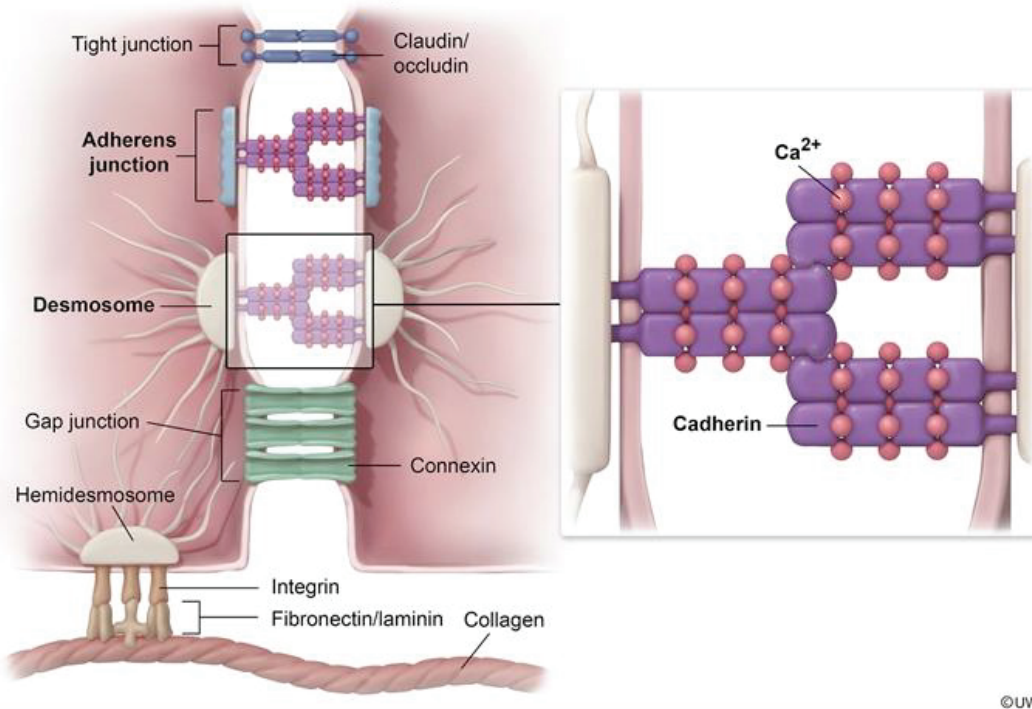
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## Cell junctions and cadherins



©UWorld

This child has a **blistering skin rash** with tan- to honey-colored **crusts**, consistent with **bullous impetigo**



©UWorld

This child has a **blistering skin rash** with tan- to honey-colored **crusts**, consistent with **bullous impetigo** (BI). BI is a superficial infection by *Staphylococcus aureus* that is most common in young children. It is spread by direct contact, with the greatest incidence in warm, humid, crowded environments. Nonbullous impetigo is a similar syndrome with pustules and crusting but without significant blistering. Either form may occur in healthy skin (primary impetigo) or broken/inflamed skin (secondary impetigo).

The blistering in BI is caused by production of **exfoliative toxin A**, a serine protease that targets **desmoglein 1** in the superficial epidermis, by some strains of *S aureus*. Desmoglein is a **cadherin component of desmosomes** in epidermal cellular junctions; disruption by exfoliative toxin A causes a loss of cell adhesion and leads to formation of flaccid bullae. Exfoliative toxin A is also responsible for staphylococcal scalded skin syndrome, which presents with generalized erythema and flaccid bullae in flexural areas.

**(Choices A and B)** Bullous pemphigoid is an autoimmune disorder associated with antibodies against hemidesmosomes and is characterized by **tense, subepidermal blisters**. Pemphigus vulgaris is characterized by intraepithelial cleavage and is due to autoantibodies against desmosomes (desmogleins 1 and 3); it presents with flaccid bullae, **desquamation**, and oral ulcerations. Both disorders cause scattered





flexural areas.

**(Choices A and B)** Bullous pemphigoid is an autoimmune disorder associated with antibodies against hemidesmosomes and is characterized by **tense, subepidermal blisters**. Pemphigus vulgaris is characterized by intraepithelial cleavage and is due to autoantibodies against desmosomes (desmogleins 1 and 3); it presents with flaccid bullae, **desquamation**, and oral ulcerations. Both disorders cause scattered or widespread (rather than localized) lesions and are uncommon in children.

**(Choice D)** Atopic dermatitis is associated with mutations in epidermal barrier proteins, leading to increased exposure to environmental antigens and immune hypersensitivity. It typically presents in infants and young children with erythematous papules and plaques involving the head, trunk, and extensor surfaces, and in older children and adults with **lichenification** in a flexural distribution (eg, neck, wrists, antecubital and popliteal fossae).

**(Choice E)** Herpes simplex virus infection is characterized by recurrent clusters of **mucocutaneous papules and vesicles** that evolve into ulcerated and crusted lesions. It typically causes localized perioral or genital lesions rather than involving large regions on the extremities.

### Educational objective:

Bullous impetigo is a superficial infection by *Staphylococcus aureus* that is most common in young





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flexural areas.

Exhibit Display

A clinical photograph showing skin lesions in flexural areas. The skin is erythematous with multiple small, raised, yellowish-orange papules and some larger, crusted lesions. A blue horizontal line is drawn across the center of the image.

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flexural areas.

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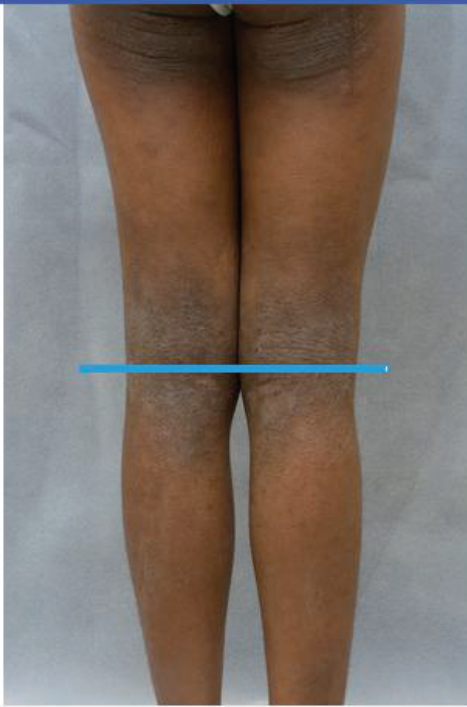


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flexural areas.

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and 3); it presents with flaccid bullae, **desquamation**, and oral ulcerations. Both disorders cause scattered or widespread (rather than localized) lesions and are uncommon in children.

**(Choice D)** Atopic dermatitis is associated with mutations in epidermal barrier proteins, leading to increased exposure to environmental antigens and immune hypersensitivity. It typically presents in infants and young children with erythematous papules and plaques involving the head, trunk, and extensor surfaces, and in older children and adults with **lichenification** in a flexural distribution (eg, neck, wrists, antecubital and popliteal fossae).

**(Choice E)** Herpes simplex virus infection is characterized by recurrent clusters of **mucocutaneous papules and vesicles** that evolve into ulcerated and crusted lesions. It typically causes localized perioral or genital lesions rather than involving large regions on the extremities.

### Educational objective:

Bullous impetigo is a superficial infection by *Staphylococcus aureus* that is most common in young children. It is characterized by a blistering skin rash with tan- to honey-colored crusts. The blistering in bullous impetigo is caused by exfoliative toxin A, which targets desmoglein 1 in epidermal cellular junctions and causes a loss of cell adhesion.

### References





A 26-year-old woman comes to the office due to a skin condition. The patient has had dry and flaky skin since childhood, but it has worsened in recent years. Her symptoms are typically worse in the winter but improve as the weather warms in the spring. The patient has a family history of asthma; both parents also have chronically dry skin. Examination shows diffuse scaling of the skin that is most notable on the extremities, as shown in the [exhibit](#). Which of the following is most likely contributing to this patient's skin condition?

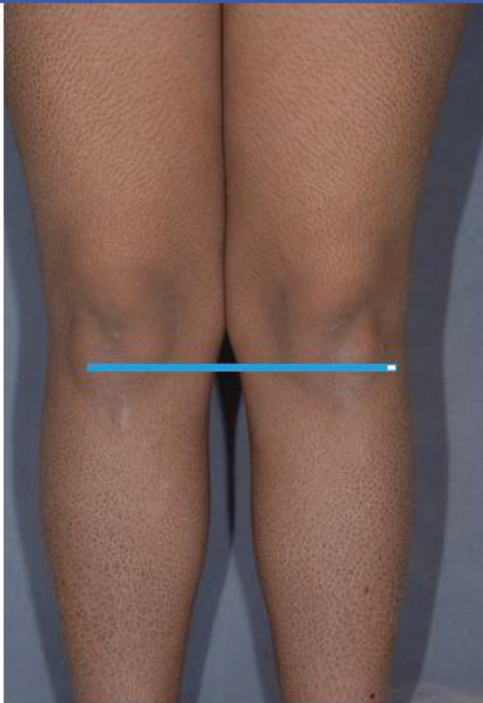
- ☐ A. Androgen-induced increase in sebum production
- ☐ B. Autoantibodies against desmogleins 1 and 3
- ☐ C. Defective keratinocyte desquamation
- ☐ D. Excessive deposition of collagen
- ☐ E. T cell-mediated inflammatory reaction

**Submit**



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A 26-year-old woman comes to the office due to a skin condition. The patient has had **dry** and **flaky** skin since childhood, but it has worsened in recent years. Her symptoms are typically worse in the winter but improve as the weather warms in the spring. The patient has a family history of asthma; both parents also have chronically dry skin. Examination shows diffuse scaling of the skin that is most notable on the extremities, as shown in the [exhibit](#). Which of the following is most likely contributing to this patient's skin condition?

- ☐ A. Androgen-induced increase in sebum production (1%)
- ☐ B. Autoantibodies against desmogleins 1 and 3 (5%)
- ☒ C. Defective keratinocyte desquamation (65%)
- ☐ D. Excessive deposition of collagen (5%)
- ☐ E. T cell-mediated inflammatory reaction (22%)

**Correct**

65%

Answered correctly



01 min, 01 sec

Time Spent



11/03/2020

Last Updated





This patient has diffuse dermal scaling consistent with **ichthyosis vulgaris**. Ichthyosis vulgaris is an inherited disorder caused by mutations of the **filaggrin gene**. This results in epidermal hyperplasia and **defective keratinocyte desquamation**, leading to the accumulation of **dry, scaly skin** with loss of normal barrier function. Filaggrin mutations are also seen in atopic eczema, and ichthyosis vulgaris is frequently associated with a family history of eczema and other atopic disorders (eg, asthma, seasonal allergies).

Ichthyosis vulgaris typically affects the trunk and **extensor surfaces of the extremities** (particularly the legs), with sparing of the flexures and face. **Palmar hyperlinearity** is also common. The symptoms first appear in childhood but may worsen with age, as well as in the winter due to decreased ambient humidity; mild symptoms may be misdiagnosed as simple xerosis (ie, dry skin).

**(Choice A)** Excessive sebum production is seen in patients with acne vulgaris and seborrheic dermatitis. Although seborrheic dermatitis presents with scaling, it primarily affects the scalp, central face, ears, and chest, and is associated with underlying **erythematous plaques**.

**(Choice B)** Autoantibodies against desmogleins 1 and 3 cause pemphigus vulgaris, which is characterized by excessive, premature desquamation. Pemphigus presents with the formation of fragile **bullae** and the shedding of epidermal sheets, rather than scaling.

**(Choice D)** Excessive collagen deposition is seen in systemic sclerosis (ie, scleroderma). Systemic





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Item 5 of 6

Question Id: 15441



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



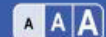
Notes



Calculator



Reverse Color



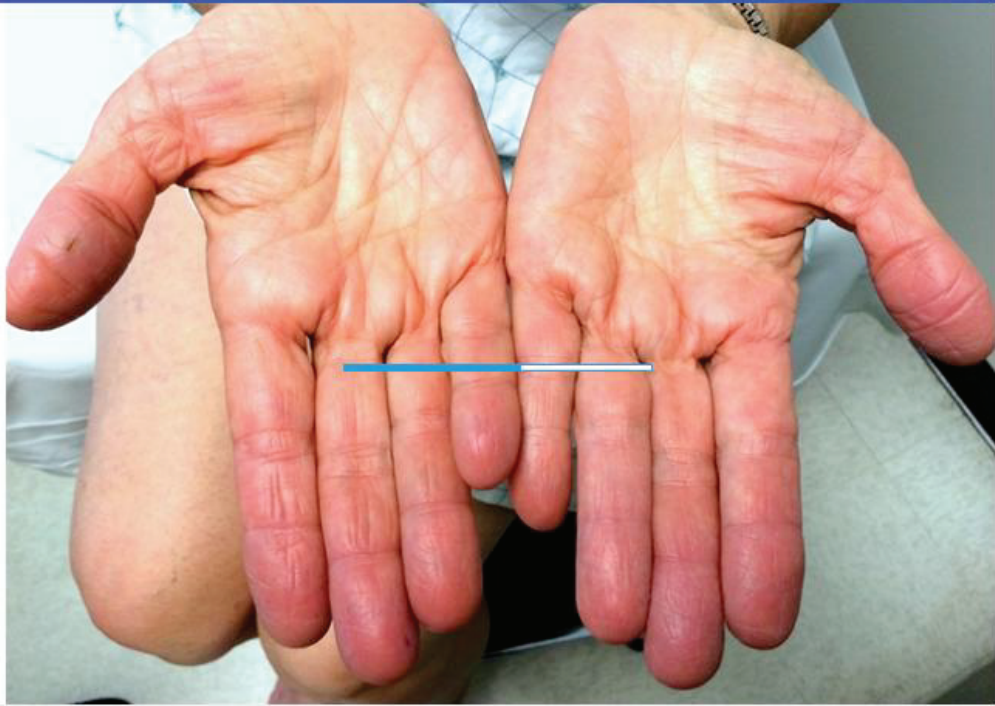
Text Zoom



Settings

This patient has diffuse dermal swelling consistent with ichthyosis vulgaris. Ichthyosis vulgaris is an

Exhibit Display



Zoom In



Zoom Out



Reset



New | Existing



My Notebook

Block Time Remaining: 00:04:32

TUTOR

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Feedback



Suspend



End Block

1  
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Item 5 of 6

Question Id: 15441



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient has diffuse dermal scaling consistent with ichthyosis vulgaris. Ichthyosis vulgaris is an

Exhibit Display



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Zoom In



Zoom Out



Reset



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End Block

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Item 5 of 6

Question Id: 15441



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

This patient has diffuse dermal scaling consistent with ichthyosis vulgaris. Ichthyosis vulgaris is an

Exhibit Display



Zoom In

Zoom Out

Reset

New | Existing

My Notebook

Block Time Remaining: 00:04:32

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Feedback



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End Block





by excessive, premature desquamation. Pemphigus presents with the formation of fragile bullae and the shedding of epidermal sheets, rather than scaling.

**(Choice D)** Excessive collagen deposition is seen in systemic sclerosis (ie, scleroderma). Systemic sclerosis presents with diffuse thickening and hardening of the skin, often associated with ulcerations at the fingertips.

**(Choice E)** Allergic contact dermatitis is a type IV (T cell–mediated) hypersensitivity reaction triggered by a variety of allergens (eg, poison ivy, natural rubber, leather dyes). It presents acutely within 2-4 days of exposure with a localized, pruritic, erythematous rash with vesicles and small bullae.

### Educational objective:

Ichthyosis vulgaris is characterized by dermal xerosis (dryness) and scaling that primarily affect the trunk and extensor surfaces of the extremities. It is caused by mutations of the filaggrin gene, resulting in epidermal hyperplasia, defective desquamation, and loss of the normal barrier function.

Pathology

Dermatology

Ichthyoses

Subject

System

Topic



1  
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Item 6 of 6

Question Id: 1108



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Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 31-year-old Caucasian female presents to your office for routine check-up. You notice several subcutaneous bumps that seem to be attached to Achilles tendons. Her father died from a heart attack at 35 years old and her mother suffers from rheumatoid arthritis. Her aunt was diagnosed with colon cancer while 55 years old. Which of the following is the best initial test in this patient?

- ☐ A. Blood cholesterol
- ☐ B. Fasting blood glucose
- ☐ C. Rheumatoid factor
- ☐ D. Antinuclear antibodies
- ☐ E. Fecal occult blood test

**Submit**

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Feedback



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End Block

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Item 6 of 6

Question Id: 1108



Mark

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Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

A 31-year-old Caucasian female presents to your office for routine check-up. You notice several **subcutaneous bumps** that seem to be attached to **Achilles tendons**. Her father died from a heart attack at 35 years old and her mother suffers from rheumatoid arthritis. Her aunt was diagnosed with colon cancer while 55 years old. Which of the following is the best initial test in this patient?

- ☒ A. Blood cholesterol (87%)
- ☐ B. Fasting blood glucose (1%)
- ☐ C. Rheumatoid factor (4%)
- ☐ D. Antinuclear antibodies (5%)
- ☐ E. Fecal occult blood test (1%)

Correct

87%  
Answered correctly

30 secs  
Time Spent

01/30/2021  
Last Updated

Block Time Remaining: 00:05:02  
TUTOR

<https://t.me/USMLEWorldStep1>



Feedback

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Item 6 of 6

Question Id: 1108



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



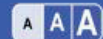
Notes



Calculator



Reverse Color



Text Zoom



Settings

Typically associated with hyperlipidemia or lymphoproliferative malignancies, xanthomas are yellow nodules composed of lipid-laden histiocytes in the dermis. Clinically, xanthomas can be divided into five categories: eruptive xanthomas (yellow papules that abruptly appear when plasma triglycerides and lipids increase); tuberous and tendinous xanthomas (the latter are often present on Achilles tendons and the extensor tendons of the fingers); plane xanthomas (linear lesions in skin folds that are strongly associated with primary biliary cirrhosis); and xanthelasma (soft eyelid or periorbital plaques with no associated lipid abnormalities in 50% of affected individuals).

Histologically, xanthomas are composed of benign macrophages packed with finely vacuolated, "foamy" cytoplasm. This cytoplasm contains high levels of cholesterol, phospholipids, and triglycerides. The lipid-laden macrophages are frequently also enclosed by inflammatory cells and fibrotic stroma. With xanthelasmas, the small aggregates of dermal foam cells are present without any surrounding inflammation or fibrosis.

**(Choice B)** Fasting blood glucose would be appropriate to evaluate in patients suspected of having diabetes mellitus or other glucose metabolic abnormalities.

**(Choice C)** Rheumatoid factor would be appropriate to evaluate in patients suspected of having rheumatoid arthritis.

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OF XANTHOMAS.

**(Choice B)** Fasting blood glucose would be appropriate to evaluate in patients suspected of having diabetes mellitus or other glucose metabolic abnormalities.

**(Choice C)** Rheumatoid factor would be appropriate to evaluate in patients suspected of having rheumatoid arthritis.

**(Choice D)** Antinuclear antibodies would be appropriate to evaluate in patients suspected of having autoimmune diseases such as systemic lupus erythematosus.

**(Choice E)** Fecal occult blood test would be appropriate to evaluate in patients suspected of having bleeding of the gastrointestinal tract.

### Educational Objective:

Xanthomas are suggestive of hyperlipidemia, especially when present in conjunction with a family history of early cardiac death.

Pathology

Dermatology

Dyslipidemia

Subject

System

Topic






A 4-month-old girl is brought to the office due to a rash on her cheeks for the past 2 weeks. The rash has not spread, and the patient is often seen scratching her face. There have been no changes in bath soaps and detergents; no animals or plants are in the house. Vaccinations are up to date. The patient is exclusively breastfed, with height and weight tracking along the 50th percentiles. Vital signs are normal. Skin examination is shown in the [exhibit](#). The remainder of the examination is unremarkable. Which of the following conditions is this patient at increased risk for developing?

- ☐ A. Coronary artery aneurysm
- ☐ B. Disabling arthritis
- ☐ C. Food allergy
- ☐ D. Proximal muscle weakness
- ☐ E. Transient anemia

  
Submit



Exhibit Display



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Zoom In

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My Notebook



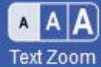
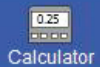
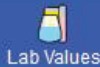
A 4-month-old girl is brought to the office due to a rash on her cheeks for the past 2 weeks. The rash has not spread, and the patient is often seen scratching her face. There have been no changes in bath soaps and detergents; no animals or plants are in the house. Vaccinations are up to date. The patient is exclusively breastfed, with height and weight tracking along the 50th percentiles. Vital signs are normal. Skin examination is shown in the exhibit. The remainder of the examination is unremarkable. Which of the following conditions is this patient at increased risk for developing?

- ☐ A. Coronary artery aneurysm (0%)
- ☐ B. Disabling arthritis (0%)
- ☒ C. Food allergy (100%)
- ☐ D. Proximal muscle weakness (0%)
- ☐ E. Transient anemia (0%)

Correct

Collecting Statistics

03 mins, 06 secs  
Time Spent03/25/2021  
Last Updated



## Atopic dermatitis

<b>Pathogenesis</b>	<ul style="list-style-type: none"> <li>• Mutation in epidermal barrier proteins (eg, filaggrin) leads to ↓ water content, ↑ permeability, ↑ inflammation</li> <li>• Immune dysfunction (ie, Th2-skewed response)</li> </ul>
<b>Clinical findings</b>	<ul style="list-style-type: none"> <li>• Acute: pruritic, erythematous patches &amp; papules               <ul style="list-style-type: none"> <li>◦ Infants: red extensor surfaces, trunk &amp; face</li> <li>◦ Children &amp; adults: flexor surfaces</li> </ul> </li> <li>• Chronic: lichenified plaques</li> </ul>
<b>Associated conditions</b>	<ul style="list-style-type: none"> <li>• Allergic rhinitis</li> <li>• Asthma</li> <li>• Food allergy</li> </ul>
<b>Laboratory findings</b>	<ul style="list-style-type: none"> <li>• ↑ IgE</li> <li>• Eosinophilia</li> </ul>

Th2 = T-helper cell type 2.

This **infant** with erythematous and pruritic patches on her **cheeks** has **atopic dermatitis** (eczema), a







This **infant** with erythematous and pruritic patches on her **cheeks** has **atopic dermatitis** (eczema), a common childhood condition that typically begins in infancy or early childhood.

The pathogenesis of atopic dermatitis is multifactorial and includes genetically mediated **skin barrier dysfunction** (eg, filaggrin mutation) resulting in loss of epidermal water content, increased permeability to environmental allergens/irritants, and skin inflammation. In addition, immune dysfunction, characterized by an underlying **Th-2 skewed response**, promotes IL-4 and IL-13 release, which stimulates **IgE production** by plasma cells.

Patients with atopic dermatitis and elevated IgE levels are at increased risk for other atopic diseases, such as **allergic rhinitis**, **asthma**, and **food allergies**. A compromised skin barrier facilitates **allergen penetration** (eg, from food) and subsequent **sensitization**, facilitating the development of food-induced urticaria and anaphylaxis. An earlier onset of atopic dermatitis (eg, infancy) is associated with a higher risk for developing these associated conditions.

**(Choice A)** [Kawasaki disease](#), a medium-sized vessel vasculitis, is associated with coronary artery aneurysms. Patients have a polymorphous rash, in addition to fever, mucocutaneous inflammation, cervical lymphadenopathy, and extremity changes (eg, edema), none of which are seen in this case.

**(Choice B)** Disabling arthritis can be associated with plaque psoriasis, which classically presents with

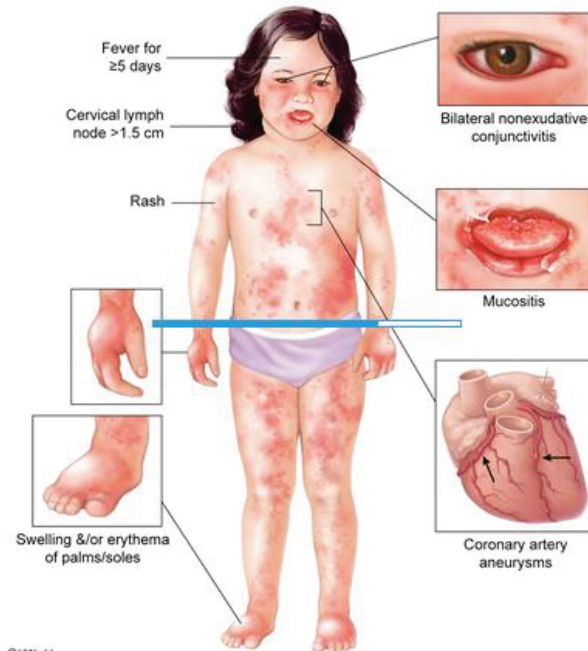




## Exhibit Display



## Kawasaki disease



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Zoom In



Zoom Out



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aneurysms. Patients have a polymorphous rash, in addition to fever, mucocutaneous inflammation, cervical lymphadenopathy, and extremity changes (eg, edema), none of which are seen in this case.

**(Choice B)** Disabling arthritis can be associated with plaque psoriasis, which classically presents with thick, **silvery scales** involving the knees, elbows, scalp, and lower back, features not seen in this patient.

**(Choice D)** Proximal muscle weakness is characteristic of juvenile dermatomyositis, which can cause facial erythema but classically presents with a heliotrope rash on the **upper eyelids**. In addition, the onset typically occurs in school-aged children, not infants.

**(Choice E)** Parvovirus B19 can cause transient anemia due to viral destruction of erythrocyte progenitor cells, typically in patients with red blood cell disorders (eg, sickle cell anemia). Initial symptoms include a nonspecific prodrome (eg, fever, coryza), followed by a nonpruritic, malar rash (ie, **slapped cheeks**) in school-aged children. This patient's age, lack of prodromal symptoms, and pruritus make this diagnosis unlikely.

### Educational objective:

Atopic dermatitis increases the risk for allergic rhinitis, asthma, and food allergies, likely because of an immune response that favors IgE production. In addition, skin barrier dysfunction facilitates food allergen penetration and sensitization, increasing the risk for food allergies.



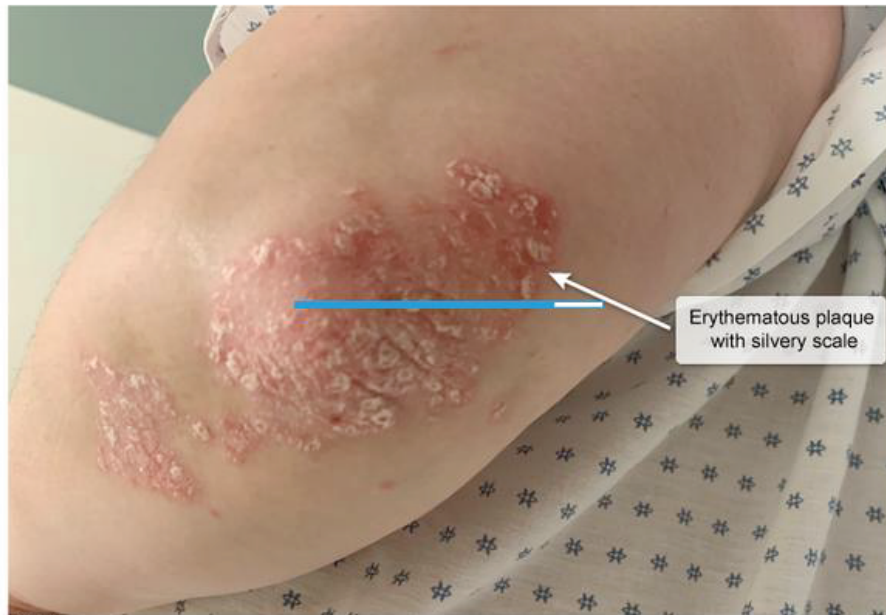




aneurysms. Patients have a polymorphous rash, in addition to fever, mucocutaneous inflammation,

### Exhibit Display

#### Plaque psoriasis



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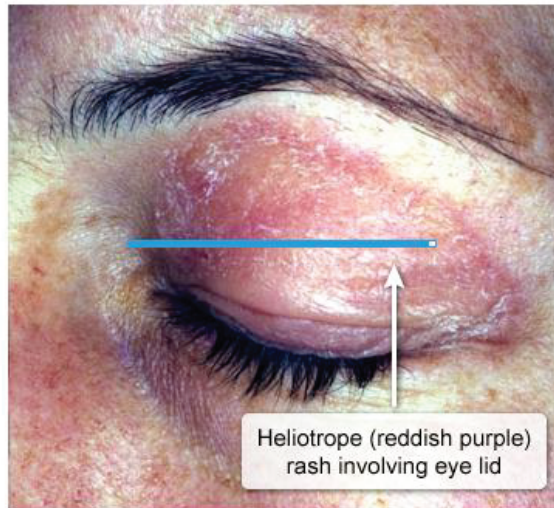




aneurysms. Patients have a polymorphous rash, in addition to fever, mucocutaneous inflammation,

### Exhibit Display

#### Heliotrope rash (dermatomyositis)



Heliotrope (reddish purple)  
rash involving eye lid

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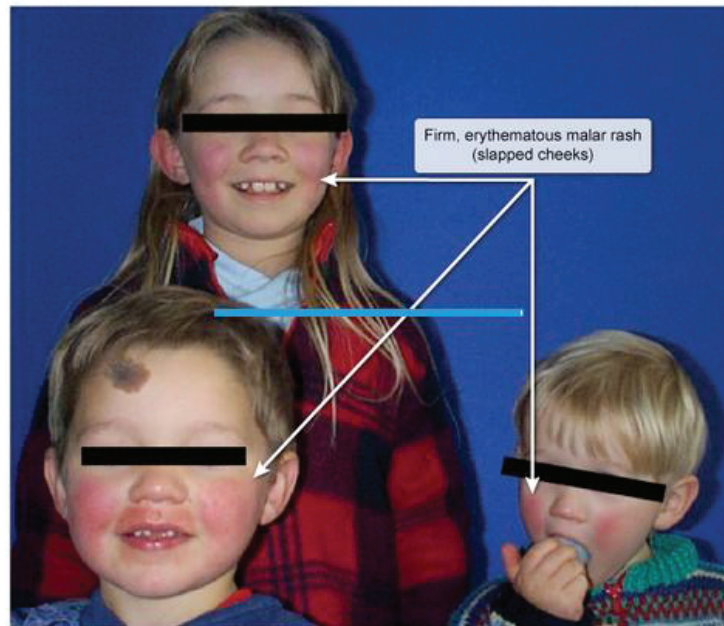




aneurysms. Patients have a polymorphous rash, in addition to fever, mucocutaneous inflammation,

### Exhibit Display

#### Erythema infectiosum



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A 6-year-old girl is brought to the clinic due to an itchy rash on her face. The patient's mother says the rash began approximately 3 weeks ago as dry skin on both of her cheeks. Over the past few days, it has progressed with areas of weeping and increased redness, and the patient has had to wear mittens to limit irritation from constant scratching. The patient has a history of similar rashes involving the flexural areas of her elbows and knees that resolved following treatment with topical corticosteroids. Vital signs are normal. Physical examination shows erythema of the bilateral cheeks and chin with crusting and oozing. The patient is prescribed a course of topical tacrolimus. Which of the following is the most likely mechanism of action of this drug?

- ☐ A. Inhibition of histamine granule release
- ☐ B. Inhibition of T-lymphocyte signaling
- ☐ C. Prevention of IgE binding to mast cells
- ☐ D. Selective blockade of the IL-4 receptor
- ☐ E. Stimulation of B-lymphocyte apoptosis





began approximately 3 weeks ago as dry skin on both of her cheeks. Over the past few days, it has progressed with areas of weeping and increased redness, and the patient has had to wear mittens to limit irritation from constant scratching. The patient has a history of similar rashes involving the flexural areas of her elbows and knees that resolved following treatment with topical corticosteroids. Vital signs are normal. Physical examination shows erythema of the bilateral cheeks and chin with crusting and oozing. The patient is prescribed a course of topical **tacrolimus**. Which of the following is the most likely mechanism of action of this drug?

- ☐ A. Inhibition of histamine granule release (0%)
- ☒ B. Inhibition of T-lymphocyte signaling (100%)
- ☐ C. Prevention of IgE binding to mast cells (0%)
- ☐ D. Selective blockade of the IL-4 receptor (0%)
- ☐ E. Stimulation of B-lymphocyte apoptosis (0%)

Correct

Collecting Statistics



01 min, 49 secs

Time Spent



03/25/2021

Last Updated

Block Time Remaining: 00:04:56

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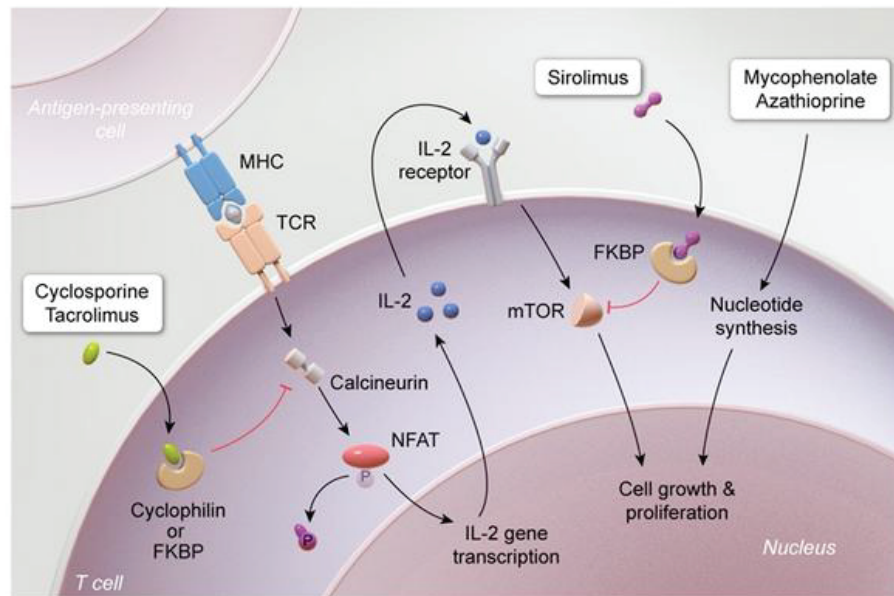


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## Exhibit Display

## Mechanism of action of common immunosuppressants



FKBP = FK506-binding protein; MHC = major histocompatibility complex; mTOR = mammalian target of rapamycin; NFAT = nuclear factor of activated T cells; TCR = T cell receptor.

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target of rapamycin; NFAT = nuclear factor of activated T cells; TCR = T cell receptor.

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PKBP = PKC $\delta$ -binding protein; MHC = major histocompatibility complex; MHC = mammalian target of rapamycin; NFAT = nuclear factor of activated T cells; TCR = T cell receptor.

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This patient most likely has **atopic dermatitis** (eczema), an **inflammatory** condition that begins in infancy or early childhood. Pathogenesis involves genetically mediated skin barrier dysfunction (eg, filaggrin mutation) and a dysregulated immune response that favors IgE production, mast cell and eosinophil activation, and overproduction of Th2 cytokines.

Loss of epidermal water content, increased permeability to allergens/irritants, and inflammation result in dry skin, intense pruritus, erythema, and, sometimes, weeping and crusting (as seen in this patient).

Distribution typically includes the face and the flexural areas of the **elbows** and knees in children.

First-line treatment of atopic dermatitis is topical corticosteroids. However, due to concerns for corticosteroid-induced atrophy in areas with thin skin (eg, face, neck, axilla, groin), second-line therapy with **calcineurin inhibitors** (eg, tacrolimus, pimecrolimus,) can be used instead. Through the inhibition of calcineurin, a lymphocyte-specific phosphatase, these medications **inhibit T-cell signaling** that would normally lead to **transcription** of the proinflammatory cytokine **IL-2**. Reduced IL-2 leads to **decreased T-cell activation** and **proliferation**, and, in turn, inflammation.

**(Choices A and C)** Cromolyn is a mast cell stabilizer that inhibits **histamine granule release** from mast cells and can be used to treat allergic rhinitis or systemic mastocytosis. Omalizumab, a monoclonal anti-

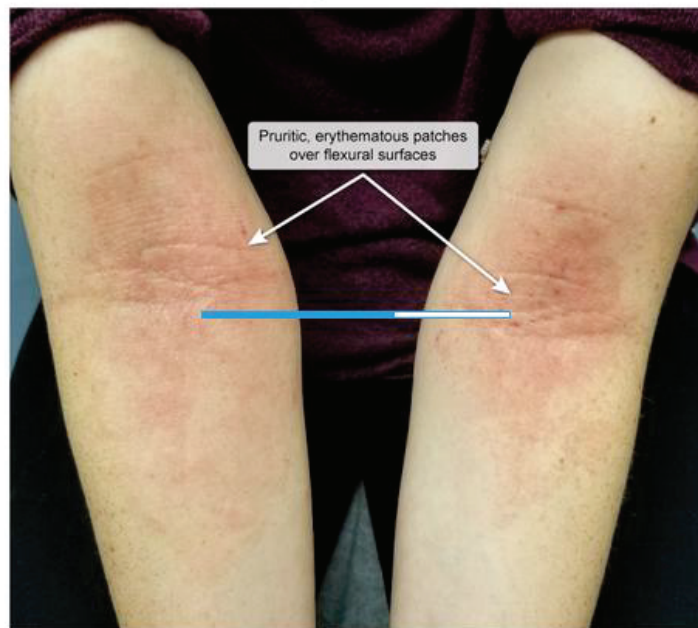




PKBP = PKC $\delta$ -binding protein; MHC = major histocompatibility complex; MHC = mammalian  
NEAT = nuclear envelope-associated transcription factor; TCR = T-cell receptor

## Exhibit Display

## Atopic dermatitis



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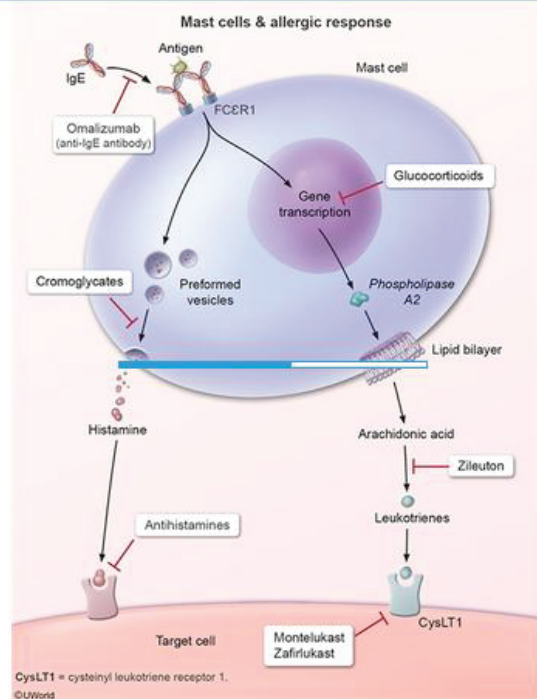


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## Exhibit Display



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**(Choices A and C)** Cromolyn is a mast cell stabilizer that inhibits **histamine granule release** from mast cells and can be used to treat allergic rhinitis or systemic mastocytosis. Omalizumab, a monoclonal anti-IgE antibody, prevents binding of IgE to mast cells and basophils and is most commonly used to treat persistent, severe asthma.

**(Choice D)** IL-4 stimulates IgE production and the differentiation of naïve CD4 T cells to Th2 cells, which exacerbate the inflammatory response in atopic dermatitis. Dupilumab is a human monoclonal antibody that inhibits IL-4 action by antagonizing the IL-4 receptor. It can be considered for severe atopic dermatitis refractory to topical therapies.

**(Choice E)** **Rituximab** is a monoclonal antibody against the CD20 antigen on B lymphocytes. Once bound, rituximab initiates complement and cell-mediated B-cell cytotoxicity. It is used to treat hematologic malignancies (eg, chronic lymphocytic leukemia) and rheumatologic diseases (eg, rheumatoid arthritis).

**Educational objective:**

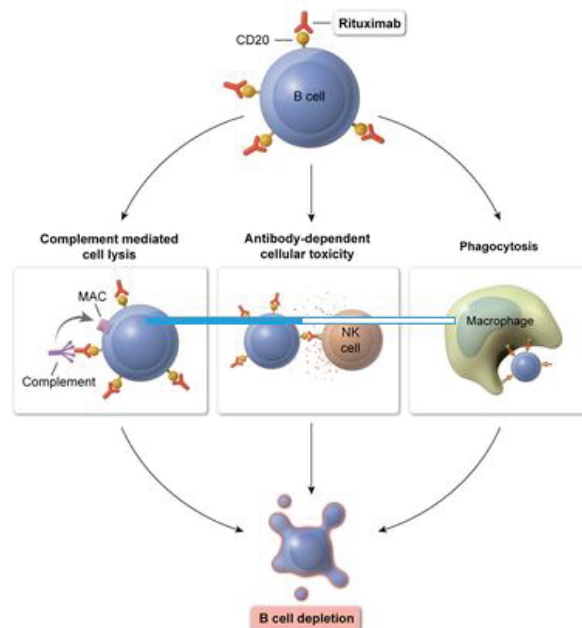
Atopic dermatitis is an inflammatory condition that can be treated with calcineurin inhibitors (eg, pimecrolimus, tacrolimus) as second-line therapy after topical corticosteroids. Calcineurin inhibitors work by inhibiting T-cell signaling needed to transcribe the proinflammatory cytokine IL-2, thereby decreasing inflammation





## Exhibit Display

## Rituximab mechanism of action



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Inflammation

Block Time Remaining: 00:04:56

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